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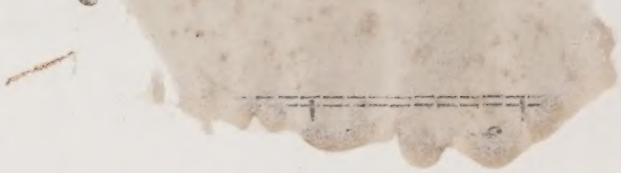

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Medicine and Mankind

Medicine & Mankind

by

ARNOLD SORSBY

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Preface

Almost each paragraph in this sketch of the conceptions and aims of medicine has a voluminous literature of its own. The futile attempt to summarize that literature has been avoided in favour of an interpretative exposition, and it is therefore obvious that there must be bias in the selection of material and in the relative emphasis on different aspects of medical activities. None the less the bias strikes no personal note; rather does it represent the point of view that pervades modern medicine.

The facts of health and disease are not isolated realities; they are aspects of life as seen from a particular angle. Where a follower of Galen could only see perfection in the human body, the modern physician often sees disharmony. The mental angle from which the body is viewed determines what is being seen. In the one case, teleology dominated all thought, in the other there is an appreciation that the body is part of the changing stuff of the universe.

With the Renaissance came the overthrow of the thirteen-centuries-old domination of Galen, and the conception that the body was a product of finished perfection—though liable to corruption—was abandoned. In the subsequent centuries less was thought of the perfection of the body and more attention was given to the manifestations of 'corruption'. In this way much solid information on the results of disease was obtained, mainly from post-mortem findings, but it is only in the last hundred years that the nature of disease, as it affects the living body, has come to be recognized. Neither the perfection nor the corruptibility of the body were seen to be significant: both these views postulated an unchanging body in a changeless environment. To-day it is clear that no understanding of health and disease is possible except through an approach which visualizes the body in unstable physico-chemical equilibrium, constantly responding to the shifting equilibria of the outer world, of which the body itself is but one aspect. It is for this reason that the study of medicine, extending as is now does to everything that pertains to the physical welfare of man, instead of being confined to the alleviation of disease must take into account not only the internal structure of man but also the outer world in which he is placed and his interactions with it. In the outer world man-made environment is no less significant than natural environment. Man, nature, and the social milieu are the trinity of modern medicine, and the three are indeed one.

This all-embracing unity is devoid of dogma or concrete shape, for the problems of health and disease are not exercises in doctrine or in statics. In a world of movement interactions between the unstable equilibria of the body and the equally unstable equilibria of the outer world do not produce a fixed product, but lead to yet another labile equilibrium with an outer world that has meantime changed too. 'Man cannot descend twice into the same stream,' as Heraclitus said 2,500 years ago; or as a modern poet has put it, 'Time has no story that's true twice in telling.' That this endless motion is not a haphazard to-and-fro, but has its own laws of cause and consequence, is clear from the orderly and relentless sequence of events in health and disease. The physician who thinks of the body as a graven image introduces idolatry into medicine. To the true physician there is no solid medium, but only motion and amorphous man.

In this sketch the activities of medicine have been reviewed in the light of these basic conceptions—not because modern medicine can somehow be forced into a mould that appeals to the writer, but because only in this way are the multitudinous activities of medicine seen to have any cohesion. If this general survey seems to embrace more than is properly the domain of medicine, the writer can only express the hope that he has interpreted faithfully, if not altogether successfully, that which is progressive and formative in his profession.

One omission calls for an explanation. Mental activities, their bearing on health and disease, and their derangements are not discussed in these pages because their complexities and significance are such as to call for more adequate treatment than could be given within the small compass of this book.

It is hoped the technical reader will forgive the inclusion of numerous and rather simple illustrations. Superfluous to him, they may be of some help to the layman, to whom they are offered by the author as an apology for the obscurity of his text.

CHAPTER I

Health and Disease

1. Disease: an aspect of life

Disease is older than man. It is coeval with life itself, for it is one of the attributes of life. Life is a labile entity in a world of flux and change, and health and disease are linked aspects of that all-pervading instability. They are the expression of an ever-changing relationship between the different components making up the living body, and between that living body and the outer world. Different working balances can be achieved in these relationships. Theoretically a body perfectly balanced within itself and to the outer world would represent perfect health, and were that balance undisturbed—by lack of internal changes and by the presence of a stable outer world—perfect health would persist into immortality. No such ideal exists in the real world, and various degrees of imbalance are inevitable. Life is always functioning under some handicap, so that 'disease' and not health is the rule. The distinction between health and disease is not qualitative but

quantitative; it is the difference between a mild and more pronounced relative imbalance, life ceasing altogether when imbalance has gone beyond one of many possible critical points. Health and disease are thus descriptive terms rather than static phenomena, and they describe states in which various factors interact to a relative harmony or a relative disharmony. Health and disease cannot be divorced from their context—the particular living organism under particular environmental conditions: being submerged under water is 'healthy' for a fish but fatal to man; man thrives in a temperate climate that is lethal to the tropical plant; the hemlock that killed Socrates is food for the goat.

Each speck of life has its own internal and external optimum conditions under which it survives and thrives, and as health and disease are aspects of these variable conditions, disease is not a direct contrast to health and much less a factor superadded to the living organism. In escaping from a plague-infested area one does not escape from disease, but from conditions unfavourable for human life, though not necessarily unfavourable to the life of a rat-flea. To the virus of smallpox the tissues of the unvaccinated individual are a favourable environment, and from the point of view of virus life the death of a patient with smallpox is merely incidental. From the point of view of human life, the discovery that smallpox virus cannot flourish in human tissues that had first been infected with-cow-pox is a triumph in the build-

ing up of an environment favourable for the survival of man.

In designating illness as ill-health and disease everyday speech intuitively reached a deeper understanding of life and its aberrations than did classical medicine, for the present conception of disease has emerged only after a break with long centuries of errors and dogmas which visualized disease as a distinct entity. And that view is still widely held. It is that view that underlies such apparently dissimilar but actually related conceptions of disease as on the one hand ascribing it to the displeasure of departed ancestors or angered gods, and on the other seeing it as the result of inimical natural forces. Whether the animistic or naturalistic view was taken, disease remained an outside force, a superadded factor disturbing human perfection. Adam of the Garden of Eden, ascribing his fall not to himself but to the tempter, may be ranked among the illustrious upholders of this dichotomous philosophy. Other champions stretch in an unbroken line, which begins in the dim ages when primitive man, bewildered in his frustrations, invoked the gods, and ends with the founders of bacteriology, whose achievement was the greatest contribution towards the enthronement of the external factor as the cause of disease, but ultimately led to the final demolition of all anthropocentric conceptions of medicine.

2. Supernatural views

The world of the primitive mind is a world of drama in which everything that happens is unexpected, for the conception of cause and effect, the remorseless logic of the consequent, is possible only to the rational mind. To the primitive mind disease had the qualities of the unexpected not so much in its existence—for disease must have been prevalent enough—as its immediate appearance. Lacking any understanding of the normal functioning of the body and all apprecation of the hammer-blows of environment in moulding and directing life, primitive man could see disease, as all other deleterious anomalies, only as evidence of malevolence on the part of an enemy. It is of little significance whether the enemy was an ill-disposed individual in their midst, a departed ancestor, an angered god, the rising moon, or the mounting storm. The irrational has its own logic, and in that logic disease was always an external force, to be overcome or else placated. Witch-hunting and veneration of the magician have the same root—the irrational mind in conflict with non-existent terrors and invulnerable nothings. Only refinement in technique, but no fundamental distinction, separates the primitive tribal ritual from the barbaric splendour of temple worship, and from the shorn glory of the present-day prayer-meeting. The Christian Scientist in the heart of London is the spiritual descendant of the native who propitiates Mumbo-Jumbo in the African jungle.

During the millennia in which the human mind had not yet reached the study of cause and effect, accidental observations and tradition evolved into empiricism, often disguised in the garb of magic. In the vast formularies of Egyptian and Babylonian medicine, no less than in the priestly codes of Leviticus, there is much that indicates careful observation and systematization of experience: copper sulphate, which is still a valuable agent in the treatment of trachoma, figures in ancient Egyptian records.

Amongst much that is pointless in these early systems there is, in fact, a core of observations that have stood the test of centuries, and this applies not only to medicinal agents but also to operative procedures. In all probability these empirical observations had the sanction of magic—procedures were regarded as effective because of their magic qualities. Yet the accumulation of empirical observations and practices inevitably led to a revaluation of the relative significance of the magic sanction and the commonplace action. Luxuriant as was the growth of magic, empiricism grew too, and it achieved a factual independence long before the Greeks definitely severed the unnatural alliance. The early associations of empiricism, do, however, emerge repeatedly in the course of its subsequent history: the medieval Arab physician, applying great skill and knowledge and invoking the name of Allah, and the medieval surgeon, who operated to a muttered paternoster, illustrate a tendency that goes back to the childhood of the race

and is never far from the surface. In our days spiritual healing is the magic formula in Savile Row clothes.

3. Rational medicine

To medicine, as to all other rational activities, the Greeks gave a charter of rights. The formative influence of Greece is well reflected in the designation of physician for the student of disease, *physis* being the Greek for nature.

Medicine owes to Greece a working method and a fallacious philosophy. The method it supplied is still the tools medicine uses today; the philosophy has been superseded, as all philosophies are superseded, with advancing knowledge. The method is clinical observation, analysis of the facts of disease with the same dispassionate care as other phenomena are studied, and interpretation of the collected data on a rational basis. Disease had ceased to be irrational and supernatural. With this approach a mass of clinical observation on the natural history of disease became available, but no amount of collected facts explains the nature of a thing. In their probing towards an understanding of the nature of disease the Greeks of necessity had to fall back upon the prevailing philosophy of the day. It is thus that they came to regard disease as a disturbance in the relation between blood, phlegm, black bile, and yellow bile, the animal counterparts of water, fire, earth, and air, the four elements of which their universe was composed. A sys-

tem of treatment emerged out of this conception of disease as an imbalance of the four cardinal elements of life. Thus venesection (blood-letting) and cauterization—both bad empirical practices—obtained philosophic sanction, and in succeeding centuries the bad philosophy of the Greeks often exercised more influence on men's minds than did their sound method of observation. In fact the method was all but lost in the decaying Roman Empire and in the Dark Ages that followed its collapse. With the Renaissance came not only a rediscovery of the Greek method but its application with a greater intensity over a far wider scale.

The Renaissance brought what Graeco-Roman medicine had hardly touched : the study, on naturalistic lines, of the healthy body, and not merely of diseased states. With the development of anatomy by Vesalius, and physiology by Harvey, clinical observations could at last be linked up with definite structures, and the theoretical needs that developed out of these speculations led quickly to the rise of the study of morbid anatomy. In the eighteenth century, Morgagni welded irrevocably the study of clinical phenomena to that of morbid changes that could be seen in the body. Clinical features were no longer studied in a sort of vacuum at the bedside, but in terms of organic changes produced during life and revealed in the post-mortem room. This was the Greek method in full flower, and unhampered by transient philosophies. In the hands of John Hunter the correlation

of clinical observations with morbid changes in organs developed into an experimental science. The vast operations of nature were studied under conditions in which the confusion of multiple causes and effects could be reduced to a more simple order by an analysis of isolated phenomena. To the mass observations on the ravages of diseases could now be added the study of reparative processes. Medicine had

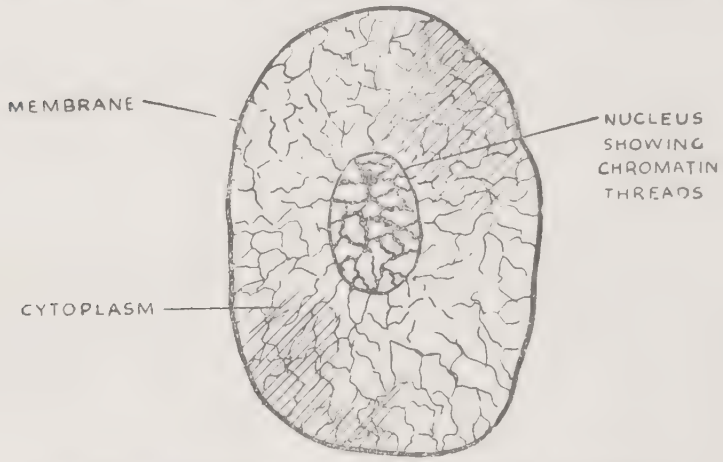


FIGURE 1. THE STRUCTURE OF A CELL

The nucleus is suspended in the cell substance (cytoplasm), which itself is bounded by a limiting membrane.

achieved the objective study of abnormal clinical states, of the normal functioning of the body, of the effects of the one on the other, and was developing an insight into the process of repair. A refinement in the study of morbid changes in organs came with the systematic application of the microscope in consequence of the recognition that the body is built up not of organs, nor of tissues recurring in different organs, but of a vast array of cells of a most diverse

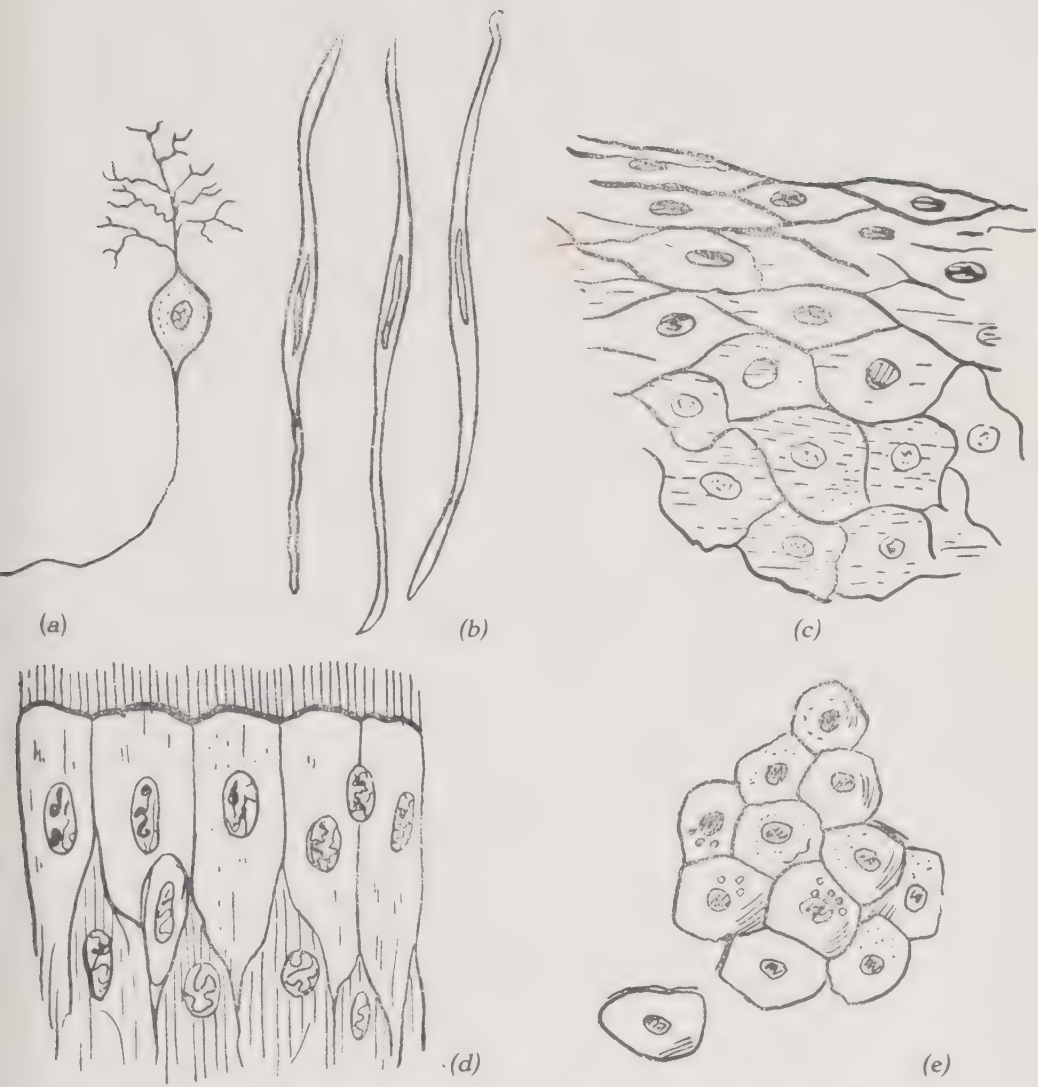


FIGURE 2. DIFFERENT TYPES OF CELLS

(a) Nerve cell. Axons and dendrons (prolongations of the body of the cell) link nerve cells to each other to form a continuous system.

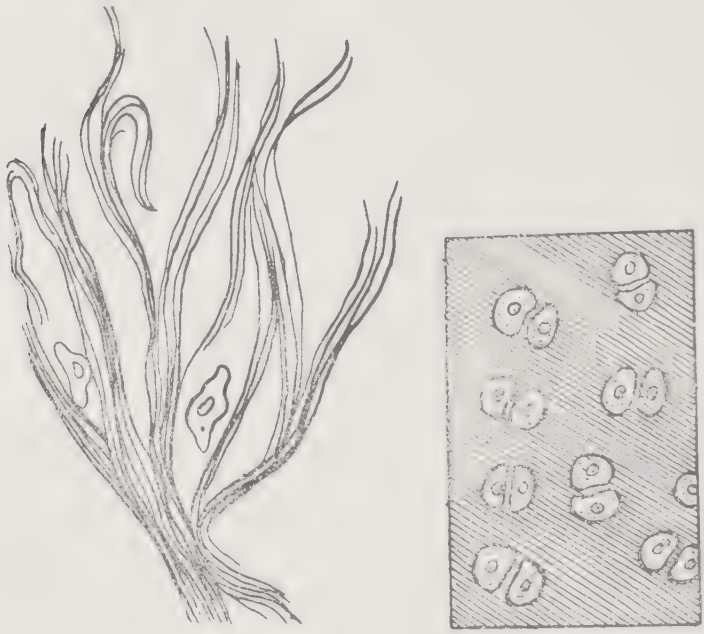
(b) Muscle cell of the involuntary type (not under the control of the will) serving the autonomic actions of the body, such as the normal rhythmic movement of the intestines.

(c) Squamous epithelial cells, essentially a lining type of mucous cell.

(d) Ciliated epithelial cells, essentially for the production and distribution of lubricating mucus secretion.

(e) Endothelial cells, particularly delicate type of lining epithelial cells.

type (Figs. 1, 2, 3 & 4). Morbid anatomy gave way to morbid histology, the ravages of disease and wonders of repair being sought with the microscope in the cells. While Morgagni saw disease in terms of



(a) (b)

FIGURE 3. DIFFERENT TYPES OF TISSUES

(a) Connective tissue. Fibres and cells acting as a binding substance for various cells and systems of cells.

(b) Cartalige tissue. A specialized form of connective tissue, constisting of cartilage cells and intermediate substance.

changes produced in an organ, and Bichat in terms of changes in tissues situated frequently in several dissimilar organs, to Virchow the secret lay in changes in the cells (Fig. 5).

4. The anatomical bases of disease

The cellular conception of disease is so far the most exhaustive basis for the classification of diseased states. The pathological changes seen in cells enable

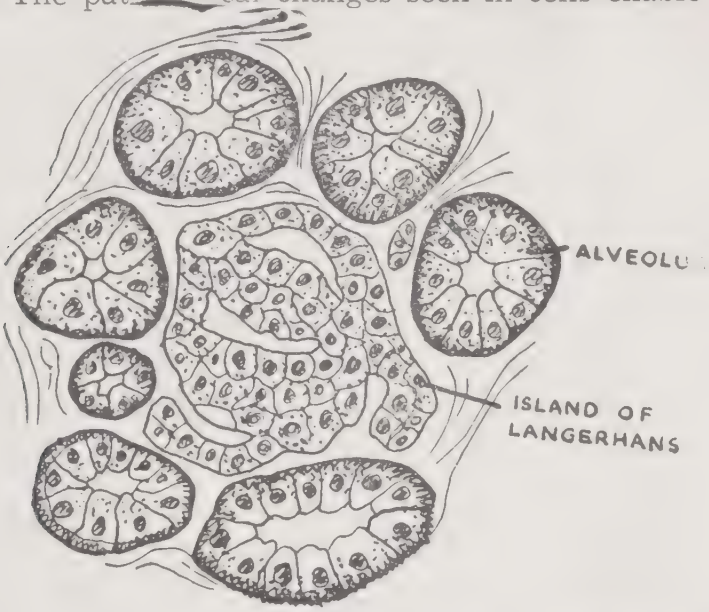


FIGURE 4. THE STRUCTURE OF THE PANCREAS AS ILLUSTRATIVE OF THE STRUCTURE OF A COMPLEX ORGAN

Epithelial cells for the secretion of pancreatic juice are arranged around a central canal into which the particular group of cells discharge their secretion. These canals converge towards the pancreatic duct, which carries the accumulated secretion into the intestine to help digestion. The unit of such a group of cells with their duct is the alveolus.

In addition to being an organ for the production of pancreatic juice, the pancreas also contains ductless groups of cells, the islands of Langerhans, which produce insulin and discharge it directly into the blood-stream for the utilization of sugar.

a finer discrimination to be made between different morbid appearances than a gross inspection of a

diseased organ allows. To the naked eye an enlarged liver may be purplish or yellowish and to the probing finger hard or soft, but a histological examination will reveal which part of the liver is affected, whether the liver tissue proper, or its supporting framework or its blood-supply. Moreover, the changes observed in the affected cells will classify the lesion in relation to similar histological changes elsewhere in the body. Thus the presence of cancer cells leads to a search for cancerous changes elsewhere, to a study of the way in which these changes make their appearance at different sites, and so to a deeper understanding of the whole problem of the origin and spread of cancer. The great variety of morbid changes observable in cells leads to a study of the different factors that produce these dissimilar pictures. The mechanism that produces congestion in liver cells is different from that which produces scarring and shrinking of the framework tissue that pervades the whole organ. Infiltration of the liver cells with fat poses the problem of the role of fats in the body, and classification of the different fats found in the morbid cell gives a clearer conception of various affections with superficially similar features, but pursuing different courses. The finding of some forms of fat in the liver cells of an individual implies a disease with a fatal course to which other members of the same family will also succumb; other forms have no such sinister significance.

A refinement of histology is the examination of the

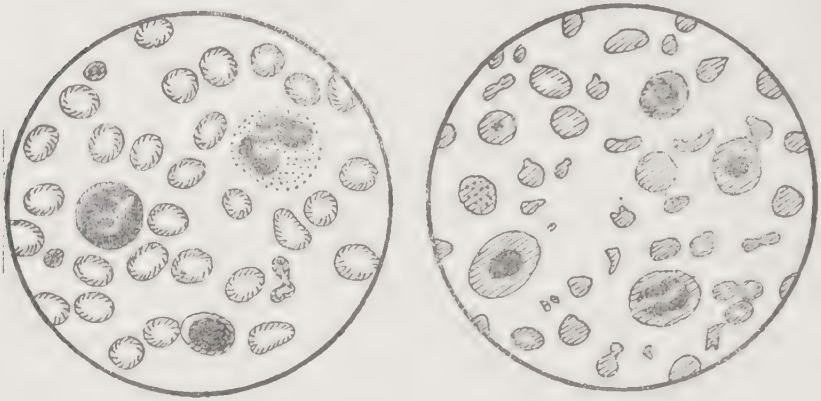
fluid tissues of the body. A blood-film made from a few drops of blood may show changes which carry a sentence of death, or indicate prognosis and methods of treatment no other approach could give (Fig. 5). The course of such an affection as meningitis and the efficacy of treatment are often best assessed by repeated examination of the cerebro-spinal fluid, not only for abnormal cells, but also for changes in its chemical composition.

As a method of description and classification the cellular conception of disease has been invaluable. It has clarified prognosis beyond the capacity of previous methods, and if 'freedom is the recognition of necessity' it has made medicine free in the sense of saving it from attempting the impossible in conditions in which experience had shown that treatment was of no avail. More significant is the guidance it has supplied in the choice of suitable methods of treatment for given cases. Thus the histological finding that a certain growth is non-malignant dictates treatment different from that dictated for a cancerous growth.

Substantial as these achievements are, they do not take medicine qualitatively beyond the achievements of the Greeks. There is of course greater knowledge, a more profound appreciation of limitations, and an infinitely greater sureness of action in fields where empirical action is effective, but real understanding of the nature of disease, its origin and elimination, is beyond any merely descriptive method.

5. The causal bases of disease

The Greek method, elaborated to perfection by the cellular conception of disease, the development of anatomy and physiology as the study of the normal begun at the Renaissance, and the broadening of the conception of life by the work of Darwin and his prede-



(*a*) (*b*)

FIGURE 5. BLOOD CHANGES ILLUSTRATIVE OF THE CELLULAR THEORY OF DISEASE

In (a) and (b) the large cells are white blood corpuscles. They are normal in both diagrams. The red blood corpuscles are of normal shape and size in (a), but show marked abnormalities, both as to shape and size, in (b). These changes are characteristic of the condition known as pernicious anaemia. In another group of blood affections (Leukeamia), the white blood corpuscles undergo marked changes in structure and in number. The course of these affections is different, and prognosis can be assessed by the blood picture.

cessors, culminated in the second half of the last century in the work of Pasteur, which for the first time gave an insight into the nature of disease. Towards its greatest achievement medicine contributed least in a direct way: Pasteur had no medical training and his first work was dictated by industrial require-

ments. The problems at issue were the chemical problem whether fermentation was a chemical or vital reaction, and the biological problem—sharpened by the then newly propounded theory of evolution—whether the lowest forms of life, such as bacteria, arise spontaneously. Having established that bacteria are not products of fermentation and putrefaction, but their direct cause, and that they are not spontaneously generated, Pasteur applied the conception to explain disease in general. A series of brilliant experiments showed mankind cause and effect in disease clearly for the first time. Infection of the living organism with a specified type of microbe, which itself could be bred pure, always resulted in a characteristic and specific sequence of clinical disturbances, and from the infected animal the original type of infecting microbe could be regularly isolated and let loose on other living organisms to repeat its characteristic ravages with monotonous regularity.

The uncharted seas of causation of disease had at length been reached, and beyond those seas lay the promised lands that would supply the means of exterminating all the ills of the flesh. With the key of causation in his hands man could confidently look forward to an age when he would utterly eliminate disease, and not merely check its ravages and counteract its effects. Having located the enemy, man felt that the battle between himself and the microbe was almost ludicrous. Successes were indeed not slow to come. Anthrax and rabies were easily disposed of,

and the technique of counteracting the microbe by producing an antitoxin to the toxin (or poison) elaborated by the microbe soon led to the preparation of vaccines, antitoxins, and sera. The elimination of tuberculosis was regarded as a feasible immediate goal, once the bacillus of tuberculosis had been isolated by Koch. In this sanguine atmosphere everything appeared foreshortened and distorted. For one thing it was overlooked that the microbe is not synonymous with disease, but that it was the interaction between the microbe and its host that produced a disordered state from the human point of view. Overlooked also was the fact that the human host was not a passive agent in the interaction between microbe and man: not all people equally exposed in an epidemic area contracted the epidemic affection. Still more fatal to an easy solution to the problems of disease was the persistent failure to find a causative organism in many affections, such as cancer and vascular degenerations—in fact in all diseases other than some fevers and allied conditions. It was of course possible to believe that a more extensive search would reveal the responsible microbe, but all such hopes had to be abandoned, and the imposing edifice of a monistic philosophy of disease came crashing down when towards the end of the century it was realized that internal disharmonies within man may produce diseased states no less than a frontal attack by microbes. It was observed that children born cretins had deficient thyroid glands, and that these

glands, far from being vestigial remains in an evolutionary sense, were essential for the normal functioning of the body; and that both in cretinism, in which the gland was defective at birth, and in myxoedema, in which it did not function fully in the adult, feeding with thyroid glands from animals overcame the 'disease'. By the beginning of the century the role of heredity in disease came to be more fully recognized, once again emphasizing the significance of man rather than his environment in the causation of disordered states. Unsuspected nutritional deficiences as causes of disease came with the recognition of the role of vitamins. Individual variations in responses to external irritants led to systematic study of the individual in relation to such irritants, and the consequent knowledge of immunity (increased resistance) and allergy (increased sensitivity) emphasized once more the significance of the host. Today it is a commonplace to say that in disease the soil as well as the seed matters, and this is but one way of saying what the centuries were slow to learn—that disease is not a distinct entity to be overcome by some medicinal philosopher's stone, some magic *Elixir vitae*, but is a series of disordered states arising under a variety of both inherent and external conditions, some clearly appreciated and easily controlled, others ill-understood and as yet beyond control.

6. Diseases as social phenomena

Diseases are not primary forces but resultant effects,

and each generation suffers not only the rulers and laws but also the diseases it inherits and merits. In the last resort particular forms of disease and their extent are not individual but social phenomena expressed through individual ciphers. It is the mode of living that moulds the formless individual imbalances of life into definite patterns of disease-processes and these patterns are ever changing, as they are largely reflections of the social background, itself constantly changing. Mental and emotional disturbances are more prevalent in times of individual and social frustration and stress; epidemics are more likely among ill-nourished populations in unhygienic conditions; chronic ill-health, with its train of acute disease, is the inevitable lot of those who attempt to live under circumstances ill-adapted for life. In life all deficiencies are relative, for an absolute deficiency of an essential component is incompatible with life, and it is the degree of relative deficiency in the sum total of the various factors that make up the physically good life that determines the particular pattern of imbalance or disease-process. It is for this reason that nutritional deficiences in Europe in its intervals of prosperity and peace give different clinical pictures from those seen in the years of depression and war, or from those seen at all times in tropical regions. Moreover, disease-patterns are influenced by geographical conditions in the sense that external factors affecting the balance of life have local characteristics; sand-flies and the infections they

transmit are not to be found in arctic regions, the humidity that favours the development of the common cold or of rheumatism is absent from the torrid zones of the earth, the hay fever induced by flowering plant life is not a winter phenomenon. The disappearance or the modification of diseases that afflicted previous generations and the constant discovery of 'new' diseases apparently non-existent before, only illustrate that disease is not one or many separate entities, malignant disembodied spirits ready to pounce on man, but is an aspect of life itself, and the endless forms in which disease appears are largely pale shadows of life's kaleidoscopic images. Though the task of the physician confronted with disease-patterns is to isolate tangible factors amenable to correction—and in so doing change the pattern of the imbalance to something less disruptive of life and well-being—disease-processes cannot be regarded as having an independent existence of their own or as possessing any final shape and form. '*Il n'y a pas des maladies, seulement les malades*' is an aphorism coined a century ago by a great clinician driven to protest against a scientific curiosity which ignored the human needs of the sick. To-day that humanitarian outlook is adamantine truth.

CHAPTER II

Health

1. Life: its limitations and instability

Life in its many and varied aspects has a strictly limited habitat. There is no adequate evidence for believing that it can be supported anywhere beyond the surface of the earth, some few miles of the atmosphere surrounding it, and a limited depth in the seas—a thin enough slice in universal space. So too with its extent in time. By human standards life has an astronomical age, but in relation to the existence of the inanimate it is very recent. To the cosmic historian life would probably be little more than the subject of a paragraph in the voluminous history of the carbon atom.

The limitations on the existence of life in space and time indicate how narrow is the range of environmental conditions under which life can function. This range is still further narrowed by the fact that working conditions and optimum conditions are not identical, and that different forms of organized life have different optimum conditions. Man is unique

among mammals in being able to exist on all parts of the earth's surface, all other mammals being more restricted by climatic and ecological conditions to limited regions. Yet even the greater freedom enjoyed by man—and much of it is the result of his own effort in evolving clothing and shelter and in establishing his supremacy against other animals—only emphasizes how narrow are the boundaries within which human life can normally exist and flourish.

In the scheme of things optimum conditions for the maintenance and survival of any particular living entity are present only exceptionally. Were it otherwise, the seas, land and air would compose one solid nightmare mass of living organisms, for the rate of reproduction is such that bacteria alone could solidify the air within days; and a limited group of fish would fill the seas with their kind, if the survival rate were anything but an infinitesimal fraction of the reproduction rate. The struggle for survival is not merely a struggle against other living forms. Survival of any particular living entity also depends on favourable meteorological conditions, access to food, and escape from the endless accidents of life. The drying of a pond will render healthy fish ill; a cold wind will take heavy toll of insect and bird life; and indirectly a parched soil will affect carnivorous animals no less than herds that subsist directly on the produce of the soil.

Optimum conditions are of course no more a static entity than is anything else in a world of flux and

change. The very mechanism of evolution is dependent upon constant changes in optimum conditions and their effect on living organisms. Health considered as an inherent attribute of an organism therefore postulates the impossible : a self-sufficient living entity. Health can be conceived only as that state in which a living organism is balanced within itself (internal balance) and in relation to the outer world (external balance).

2. The internal balance

The internal balance of man is a complex process. The life activities of the individual cell are tangled beyond our understanding, and man is more than a conglomeration of cells. He is an integrated being in which the cells are systematized into organs with functions surpassing those of the component cells; and the organs themselves subserve a series of autonomic actions to maintain the life of the body as a whole, which in turn is the instrument of man's conscious and purposive activities.

Under maintained optimum conditions the life process of a cell can apparently continue indefinitely. With adequate nutrition simple cells (such as fibroblasts) can multiply and remain alive indefinitely. With more complex nutrient media, such as extracts of embryonic tissue, undifferentiated (simple) cells may not only grow but also develop into specialised forms (differentiation). Young cells give better results in these laboratory experiments than do adult cells,

and embryonic tissues are best. To what extent the adult cell is actively damaged by its previous life, or inherently incapable of the achievements of an embryonic cell, cannot be clearly established. Fundamental as this issue is, the important fact emerges that given favourable conditions the survival capacity of the cell is immense. The cell may well be immortal, but what is just as significant is the sensitiveness of the cell to an unfavourable environment. Life is no more its inalienable prerogative than its decay due to malfunction and death are an inescapable curse.

What applies to cells may perhaps also apply to organs, which in one sense are systematized colonies of cells. The brilliant work of Carrel has shown that, given exquisite care in supplying satisfactory conditions, organs like the whole heart or the whole kidney or thyroid gland can be kept alive outside the body and studied for their response to the addition of noxious substances or the deletion of essential factors in nutrition. The 'health' of such preserved organs is readily affected.

Cells and organs have thus a considerable stability matched only by the ease with which they succumb to deleterious external conditions. Evolution, however, has produced not only the endless complexity of multicellular organisms, but also a controlled environment within the body (internal environment) giving greater protection to cells and tissues than the outer world gives to the unicellular organism exposed to the ceaseless changes going on around it. This

favourable internal environment is not something given, but is a perpetually re-created set of conditions, involving specialization and interaction of the various cells.

A constant temperature, a narrow range of alkalinity, a steady supply of nutrition, and a ceaseless removal of waste-products, are the immediate requirements of a cell; for its proper functioning it must also be able to draw upon stored energy for exceptional conditions. All these the multicellular organism supplies by the intricate process of co-ordinated action of the cells throughout the body. A failure in this co-ordination is a failure in 'health'.

A constant temperature in man is achieved by the complex mechanism of heat-regulation. All animals except mammals and birds are cold-blooded in the sense that the temperature of their bodies corresponds to that of the environment. Since life is possible only within a narrow range of temperatures, and the activities of tissues are influenced by heat and cold, it is obvious that the cold-blooded animal is more exposed to deleterious environmental conditions than is the warm-blooded organism with its constant internal temperature (steadily maintained despite a considerable range of variations in external warmth). Controlled heat production and heat loss are necessary for the maintenance of a constant temperature, and its achievement is an excellent illustration of the integrative action of the body as a whole (Fig. 6).

The main source of heat production is muscular

activity. In the cold-blooded animal muscular activity, as all other activity, decreases when the external temperature falls, but in the warm-blooded animal external cold is counteracted by the internal regulating mechanism, which stimulates bodily activity and thus raises the body temperature. Shivering in extreme cold is an illustration of increased muscular

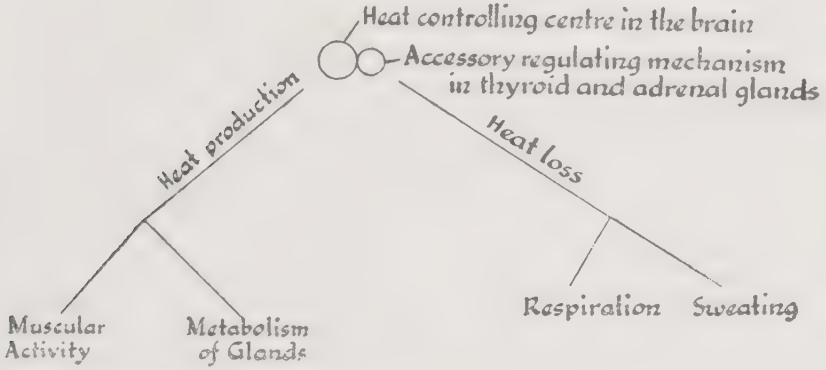


FIGURE 6. HEAT REGULATION

Scheme showing heat controlling centres keeping the body temperature constant by regulating heat production and heat loss.

activity whereby heat production is increased. Loss of heat is achieved mainly by the lungs and skin. Increased respiration and the consequent increased loss of heat from warming a greater amount of expired air is seen in the panting dog on a hot day. In man sweating serves a similar function, and flushing of the skin after exercise is but the same process in a minor degree, as is the normally slight moistness of the skin. The means whereby these regulating mechanisms come into operation involve the activity

of a centre in the brain (in the hypothalamus) and the action of the thyroid and suprarenal glands. When blood of a temperature different from the normal reaches the hypothalamic centre, nervous stimuli cause the blood-vessels of the skin to dilate or contract and heat loss is thus controlled to the necessary extent. The roles of the thyroid and suprarenal glands are seen in the greater output of their respective secretions on a decline in temperature; these secretions chemically stimulate the chemical processes in the tissues generally and so increase heat production; adrenalin (derived from the suprarenal gland) also constricts the skin blood vessels and so diminishes heat loss.

The complexity of this process illustrates the high degree of specialization and integration necessary in cells and organs to overcome—though only partially —man's dependence on such an isolated external factor as temperature: nervous regulation through the brain, chemical regulation through the ductless glands, the activities of the muscles, skin, and lungs are all called into being.

Similar complex mechanisms and regulating activities operate to ensure a stable environment in the alkalinity of the tissues, and in their nutrition. All cells are bathed in body fluids, from which they derive their nourishment. These fluids are derivatives of the blood, which must be maintained at a fine point of alkalinity if life is to continue at all. The amount of hydrogen ions in the blood is almost incon-

ceivably small, being 0.000000032 gr./litre (1 gramme ion in 32 million litres of blood). Slight variations have profound effects; thus breathing becomes appreciably affected if the concentration rises to 0.000000034, and is greatly embarrassed at 0.00000005. The self-regulating mechanism in the body whereby the alkalinity of the blood and tissues is preserved includes a complex series of autonomic acts which involve (1) a response of the breathing centre in the brain to slight changes in the hydrogen-ion concentration in the lungs, inducing deeper respiration when there is an excess, so that gaseous acid is washed out from the blood; (2) a buffer action of alkaline substances in the blood which absorb excess of acid; and (3) a change in the reaction of urine as a result of the excretion of the surplus acid or alkali.

The nutrient substances carried by the blood have similarly to be kept within physiological limits. Calcium, iron, phosphorus, and other elements are essential in sufficient quantities for proper functioning of tissues and all act deleteriously in excess. Intake and excretion are finely balanced.

The endless adjustments and readjustments in the body, aiming at a stable internal environment restricted within narrow limits, illustrate the complexities of integration in the multicellular animal. The specialization of cells to form nervous tissue, ductless glands, digestive and excretory organs, and all the other manifold variety of tissues with a specific purpose may be regarded as Nature's attempt at making

life less dependent on the outer world. Nothing approaching independence is of course achieved, but the survival value of the multicellular animal is greater than that of the unicellular organism. Yet life still remains unstable and not self-sufficient. For its somewhat diminished dependence on the outer world the price is the maintenance of a delicate balance within the integrated cell colonies.

3. Changes in balance

That balance not only flutters with every wind of circumstance, but has changing optimum conditions dictated by the different phases of life and their activities. The increased rate of the heart and the rise in blood-pressure that occur with physical exertion are an essential adjustment, for it is in this way that the body can produce the necessary additional mechanical energy and the tissues are enabled to function. Normally the heart propels into the body six to seven litres of blood per minute, but this rises to as much as thirty litres per minute in violent exercise. Such a quickening of activity is necessary for the supply of nutrition and oxygen to the tissues and involves a corresponding adjustment in the excretion of waste products. Failure in adjustment or in maintaining an adjustment that has been reached renders the task attempted impossible. If, in the first place, sufficient energy is not liberated by the adjustment initiated by the desire to undertake the work, the task cannot be undertaken at all; and if there is

a failure in the excretion of the waste-products of muscular activity, lactic acid—one of these products —accumulates in the muscles, inducing the sense of fatigue.

What happens with heart-rate and blood-pressure during exertion also happens in many different ways with other functions of the body, and some of these functions call not for transient readjustments, but for prolonged changes. The needs of the growing child differ markedly from those of the adult: its developing bones call for a greater amount of calcium and phosphates, which are essential for the growth of bone. The expectant mother needs a larger amount of iron, if both she and her offspring are not to suffer from a particular form of anaemia (nutritional anaemia). The lowered digestive capacity of the aged is in part, at least, an adjustment arising from their lowered capacity for action, itself due to a variety of causes.

All this illustrates forcibly enough that what would constitute health at one period would be abnormal at another. This is still further instanced in the fundamental antithesis between growth and specialized function. The embryonic cell is undifferentiated: it has the capacity to develop into a variety of tissues. In its undifferentiated state the chief activity of the cell is growth, and under experimental conditions growth of such cells may be continued indefinitely. Growth becomes a subsidiary feature or ceases altogether when such cells are allowed to

develop into specialized cells subserving a definite function: the embryonic cell that has developed into, say, nervous tissue functions as such and shows but relatively little capacity for growth. The change that has occurred is of such a character that not only are a new set of conditions necessary for the healthy functioning of the specialized tissue, but a definite antagonism to the previous conditions has developed; if extract of differentiated or adult tissue is added to the nutrient medium in which the embryonic tissue was growing freely, growth is inhibited. The health of the adult tissue is poison to the embryonic cell.

4. Environmental influences

Presumably life in its lowest and highest forms is fundamentally the same, and amidst the endless varieties of form some inherent character determines the particular form. Under no conditions will the ovum of a frog develop into a man; and no matter how much difference exists between different men, the common form of humanity will be present. This inherent characteristic makes towards stability in an otherwise unstable world. Yet even this tentative stability has strict limitations. It is possible that human races of pygmies and of tall people, and equine races such as the small Shetland ponies and the breed of great Clydesdales, may have been evolved by environmental conditions, but it is more likely that inherent factors are responsible for the differences, for the basic stature of a species, though

influenced by environmental factors, is largely determined otherwise. But a much greater range of stature and weight than that shown by men and horses is seen arising from purely environmental conditions in the case of fish. 'Good waters' have large fish and 'poor waters' have small fish: in certain lochs in Scotland the mature trout—though plentiful—are all about a quarter of a pound in weight; in other lochs they grow much larger, some to weigh twenty to thirty pounds. The great range in size and weight that the animal and plant breeders can produce by selection and inbreeding illustrates the essential instability of the 'inherent' factors.

'Inherent' factors are in the long run the relatively stable features produced in the course of evolution, and they too are part of the changing pattern of all existence. The instability of the external environment, of the internal environment and of 'inherent' factors thus negate any attempt at defining health in static terms.

Health is not a gift of the gods, to be held once granted; it is an ever-changing balance of forces, which conscious, purposive man can support or disturb, but cannot disrupt without destroying himself.

CHAPTER III

Disease: The Ill-Formed Body

1. Racial inheritance

The new-born child does not start life afresh. He is incredibly old, carrying on his frail shoulders an endlessly remote racial inheritance and a more immediate parental legacy. By virtue of his racial inheritance he is man; his parental legacy makes him the man he is.

An older generation of biologists, the contemporaries of Darwin, spoke of man as climbing his own family tree. They saw in the progressive unfolding of embryonic development a repetition of man's slow ascent on the evolutionary ladder, regarding the unfertilized ovum as the unicellular stage, the fertilized ovum as the beginning of the multicellular organism, and the increasing complexities of embryonic development as representing different stages in evolution, culminating in man at the end of embryonic life. The nine months of human gestation were thus regarded as a highly telescoped replica of human evolution. In broad outline this picture is true, for

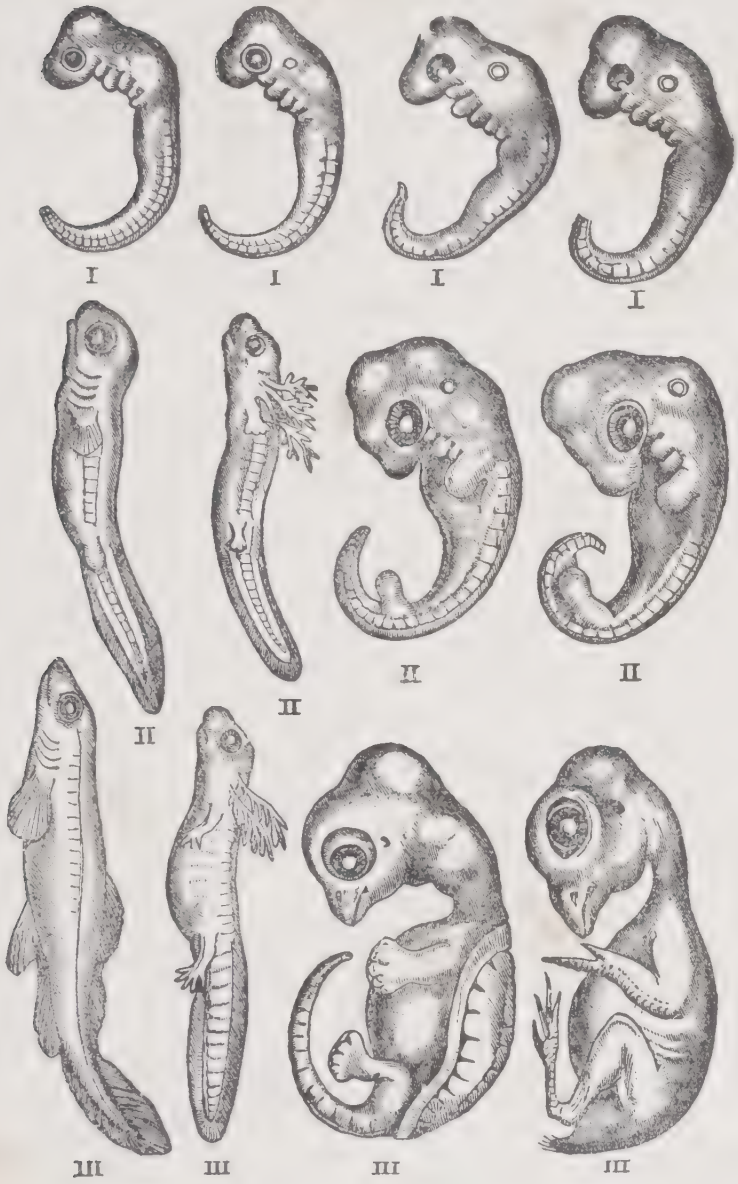


FIGURE 7. (*a*) EMBRYONIC DEVELOPMENT

A series of embryos at three comparable and progressive stages (marked I, II, and III) representing each of the classes of vertebrate embryos below the Mammalia.

FIGURE 7 (*b*)

Another series of embryos, also at three comparable and progressive stages of development, representing four different divisions of Mammalia.

Note the striking similarity of the embryos at Stage I, beginning with the Fish in Fig. 7 (*a*) and ending with man in Fig. 7 (*b*).

various stages of embryonic development do indeed testify to man's origin from more lowly forms of life (Figs. 7 & 8). The segmentation of many primitive forms of life is strikingly preserved in the embryo at the stage when five gill-slits in the neck repeat

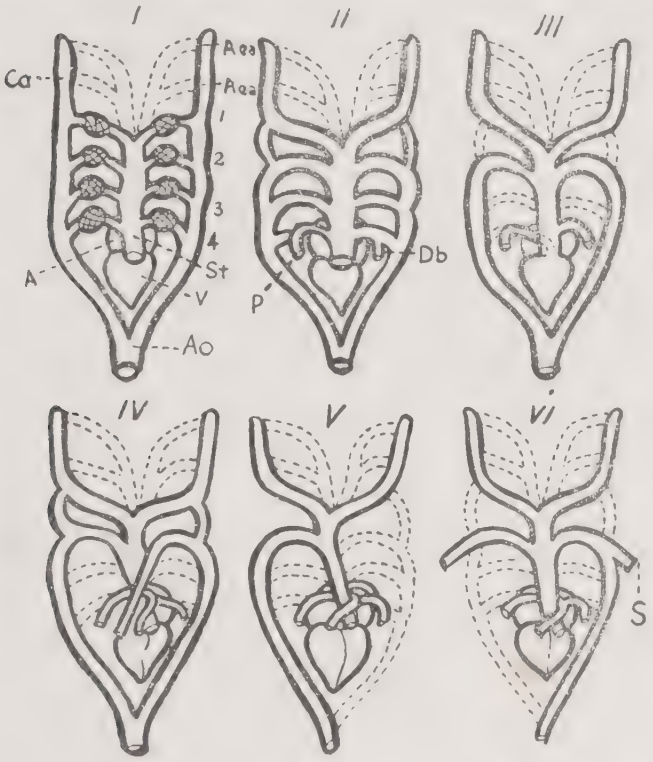


FIGURE 8. THE TRANSFORMATION OF THE BLOOD-VESSELS IN THE GILLS OF A FISH INTO THE PATTERN SEEN IN MAN

The diagrams I-VI represent the circulation of a fish, reptile, frog, lizard, bird, and a mammal respectively. The blood-vessels that disappear in the more complex animals are shown by dotted lines. In the adult mammal (VI) relatively little remains of the primitive pattern seen in (I), though the mammalian embryo repeats that pattern faithfully at an early stage.

the normal appearance in the fish; these gill-slits persist in man, though in a highly modified form (Fig. 9). The first gill-cleft becomes the Eustachian tube of the ear, and, as Darwin pointed out, we carry in our ears and ear-passages unmistakable evidence of our aquatic ancestry.

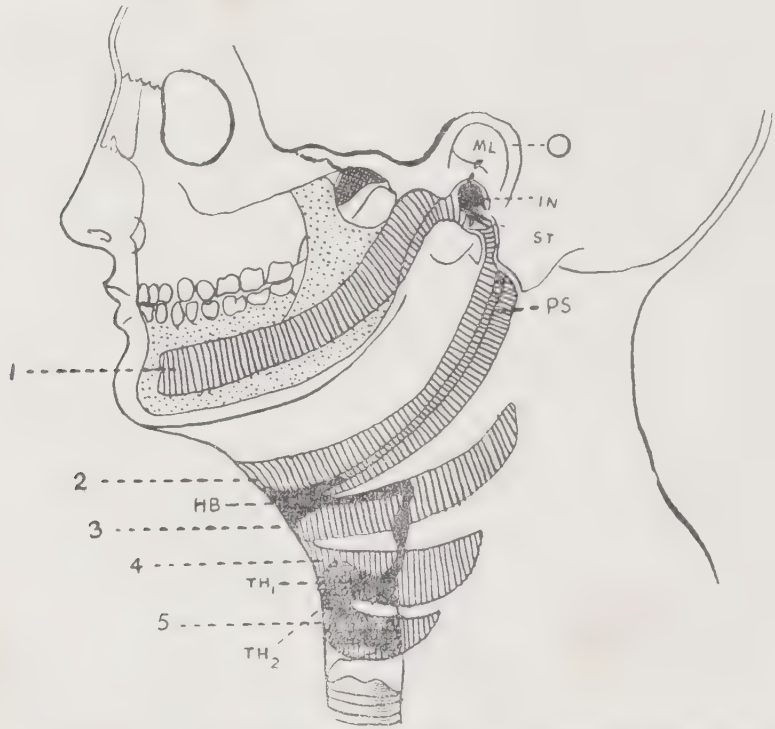


FIGURE 9. REMAINS OF GILL ARCHES IN MAN

1-5 represent the primitive gill arches seen in the fish. The small bones of the ear (ml. the malleus, in. the incus, and st. the stapedius) develop from the cartilage of the first arch. The cartilage of the second to fifth arches form the hyoid and thyroid cartilages in the neck.

Under the impact of the theory of evolution the second half of the last century tended to see useless vestigial remains in many human organs that were ill understood. Man's body is indeed a store-house of ill-

adapted ancestral organs, but hardly to the extent that was previously believed; a cluttering up with purposeless relics would have eliminated man in the struggle for existence. True, man's sparse hairy coat is useless to him, but it is a legacy that constitutes no handicap; his useless plantaris tendon becomes a nuisance only under exceptional circumstances. The recognition of these minor disabilities is, however, a different matter from such extreme views as that which saw useless vestigial remains in what are now recognized as vitally necessary organs, such as the thyroid gland.

Man's lowly ancestry may, however, contribute directly towards malformations. The failure of a gill-cleft to reach its full human transformation produces a series of congenital abnormalities ranging from fistulae (openings) in the neck to cysts which later may be the seat of cancer. A failure in the full development of the heart may produce a condition that is normal for the reptile, but lethal or highly embarrassing to man, and constitutes one form of congenital heart disease. Congenital dislocation of the hip is a crippling condition to man (or rather to woman, for it affects women rather than men), but is normal and very well adapted to the waddling reptile.

Arrest of development is commonly associated with some aberration (development of additional and abnormal tissue), and several forms of congenital abnormalities of the kidney show aberrant developmental changes which themselves lead to grave consequences

to the body economy as a whole. Thus arrest in kidney development may be associated with the formation of a tumour incompatible with life of any duration. In one sense malformations are a time scale of human evolution, for it may be taken as a general rule that the older a structure is in the evolutionary sense (phylogenetic age) the less likely is it to show developmental anomalies in man.

If man's racial inheritance makes him man, a flaw in the title-deeds may make him less than man. Serious defects are incompatible with life and may be a cause of miscarriage during pregnancy; less serious failures give a whole range of abnormalities, extending from non-viable (still-born) monstrosities on the one hand to minimal defects such as Darwin's tubercle on some ears—the remnant of the pointed ear of a more lowly ancestor.

2. Parental inheritance

The immediate parental legacy determines the thousand and one ways in which individuals differ from each other and is a much more fertile source of congenital abnormalities and disease than racial inheritance. Parental legacy operates in two ways in the moulding of the individual. In the first place the individual at the stage of fertilization of the ovum derives inherited characteristics—good, bad, and neutral—from both his parents. Secondly, during his period of development from ovum to birth he lives in the secluded environment of his mother's womb and is liable

to an endless series of influences deriving from the mother.

The inherited characteristics of the individual have been the subject of extensive and far-reaching studies in recent years. That both desirable and undesirable features can be inherited has, of course, been known for centuries, and this knowledge has played a great social role in history. It has buttressed up such philosophies as the divine right of kings and has given support to the strangle-holds of priestly castes, the arrogance of the feudal nobility in the Middle Ages and of the 'good families' and 'master races' of our day. Behind all these conceptions lay the belief that given qualities are inherent and permanent in different sections of the human race, and that 'goodness' and 'badness' are transmitted as such. That accidents happened in the best families was indeed recognized, but these were regarded as the exceptions that proved the rule—a rule which overlooked the all-important fact that heredity is an innovating as well as a stereotyping force.

That the mechanism of inheritance operates according to simple rules was first established by Gregor Mendel in 1866, but his work was overlooked until it was re-discovered independently by Bateson and De Vries at the beginning of the century. Since then not only the 'rules' but the very mechanism of heredity have been laid bare. The gene theory of heredity, as evolved by Morgan, localizes hereditary features at hypothetical points ('genes') in the microscopically

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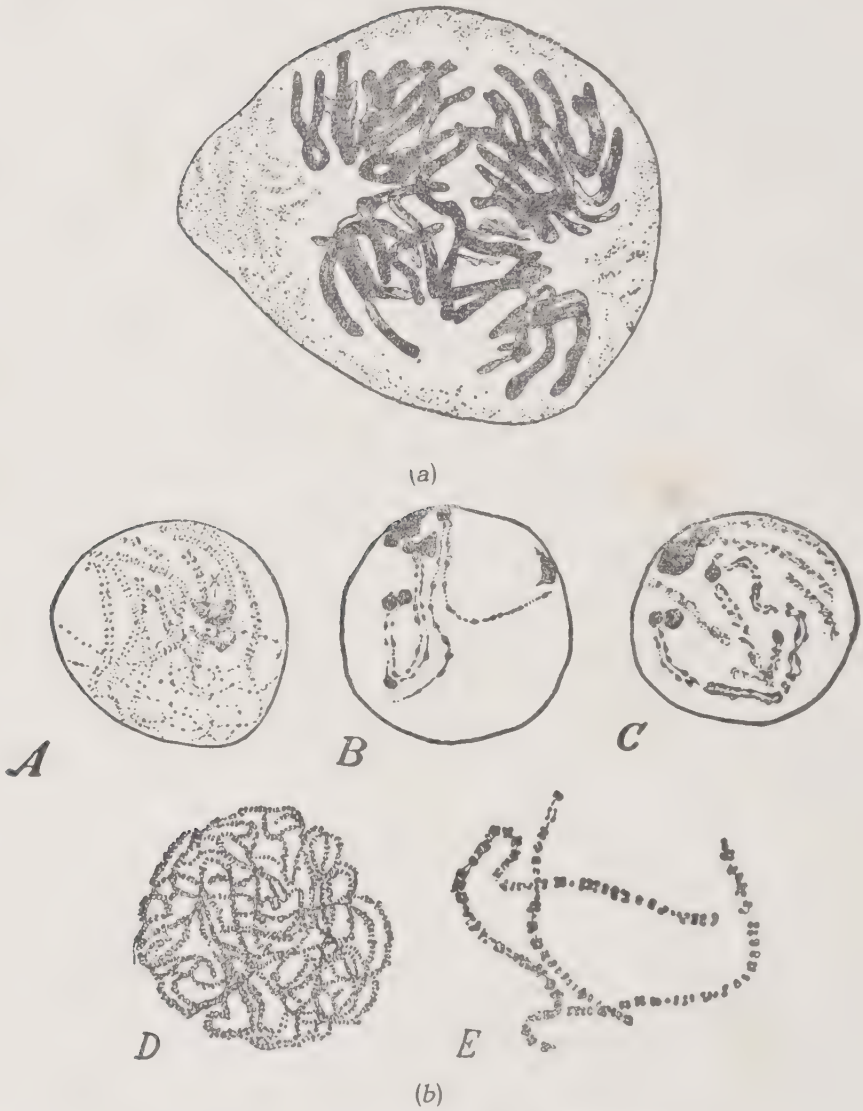


FIGURE 10. CHROMOSOME STRUCTURE

(*a*) Chromosomes in a dividing cell (of a salamander).

(*b*) Structure of chromosomes as seen under the microscope. The minute paired particles (chromomeres) are clearly seen and probably represent the genes. In B the two members of one chromosome pair are approaching each other in conjugation, but are not completely conjugated. E shows a portion of D at a higher magnification.

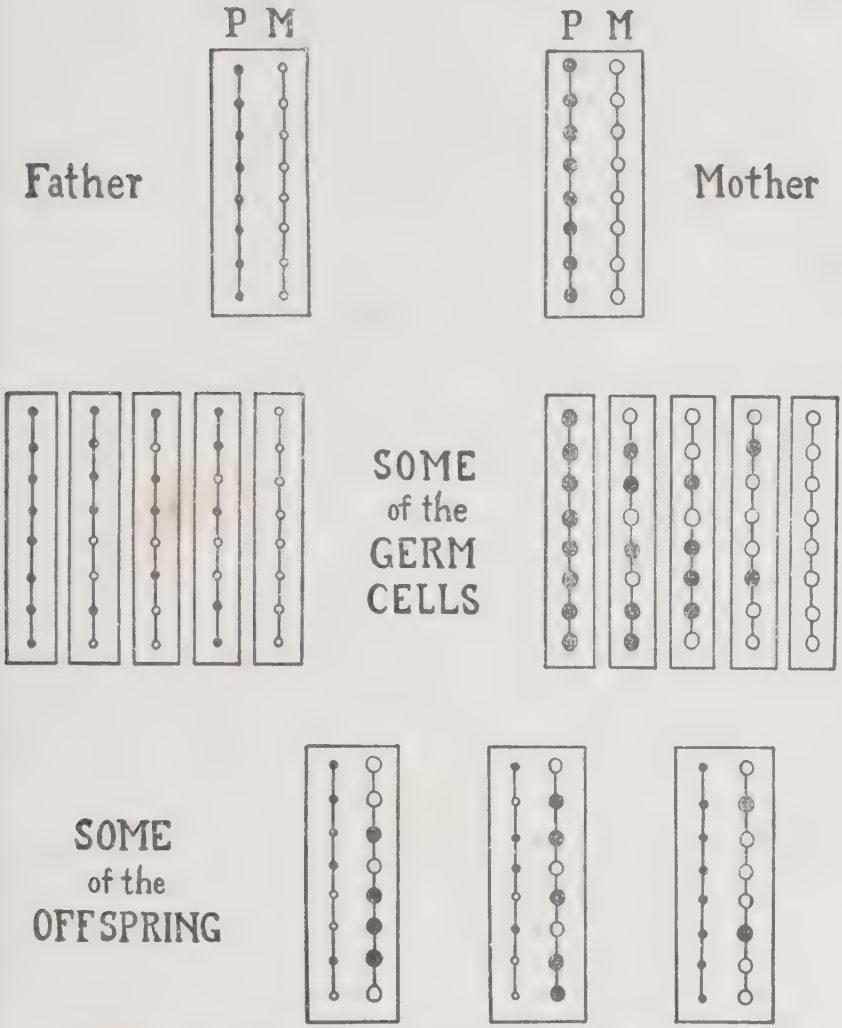


FIGURE 11. THE REDISTRIBUTION OF GENES IN REPRODUCTION

In each of the two parents are strings of genes, paternal (P) and maternal (M), represented respectively in black and white. These genes from both parents are distributed to the germ cells in all possible different combinations (as indicated in the sample germ cells in the centre of the diagram). The offspring which develop from the combination of these various germ cells present a still greater possible range of characteristics.

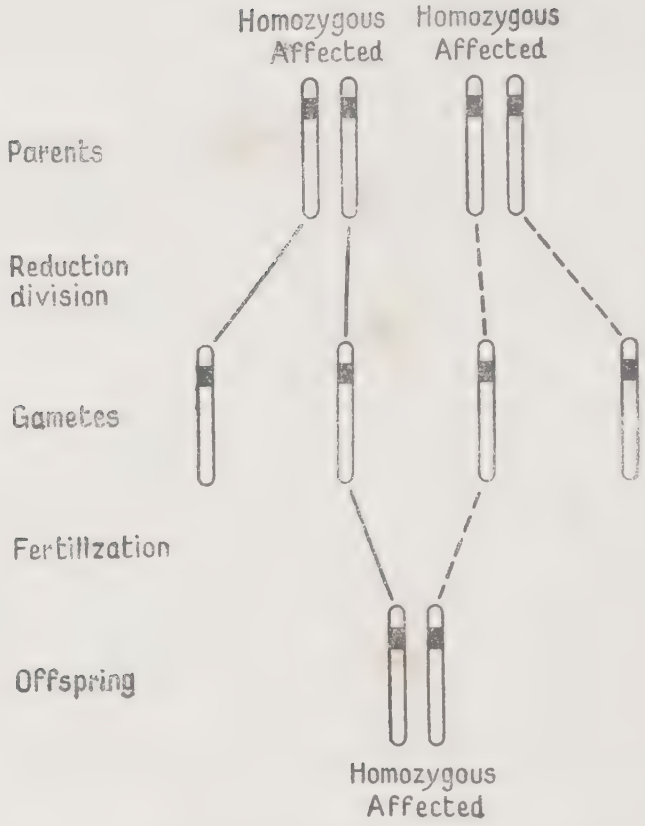


FIGURE 12 (*a*). GENES IN INHERITANCE

In these diagrams the gene carrying one abnormality is shown as black in the drumstick figure which represents a chromosome. A person is spoken of as being homozygously affected if both his genes for the particular characteristic are abnormal (in the same way); he is regarded as heterozygously affected if only one gene is abnormal. In reproduction there is first a dissocation of the two genes determining the characteristic in each of the parents. In the constitution of the new individual any two of the four dissociated genes may enter, resulting in a variety of patterns.

With both parents affected in both genes all children must be abnormal, irrespective of whether the affection is recessive or dominant, as there are no normal factors to be expressed. (Likewise with both parents normal in both genes, there is no possibility of hereditary disease.)

observable chromosomes within the nucleus of the reproductive cells (ovum and sperm) (Fig. 10), and the behaviour of these genes can be predicted with mathematical accuracy. In all features a character is determined by at least two genes, each of the parents having contributed one (Fig. 11). Where both genes carry no abnormality, the resultant feature cannot be abnormal, from the hereditary point of view. Should one gene carry an abnormal character, this may or may not become apparent in the individual, depending upon its being 'dominant' or 'recessive' (Fig. 12 *a*, *b*, *c*, *d*, and *e*). It becomes apparent where the abnormal gene is dominant in relation to the gene carrying normality. It does not become apparent if the normal gene is dominant to the abnormal one; but under such conditions the individual, though healthy by clinical standards, is genetically diseased in the sense that the abnormal factor he carries may become manifest under suitable conditions in a subsequent generation. What happens is that in transmitting these genes—for the genes constitute the hereditary material transmitted from generation to generation—both the normal (in this case dominant) gene and the recessive gene are handed down, not combined as in the parent cell, but dissociated. Should a recessive (and therefore non-manifest) gene become combined during the formation of a new individual with a gene carrying the same abnormality—i.e. should both parents carry recessive genes for a particular abnormality—the new individual, instead

of having one recessive gene with an abnormality overcome by a dominant gene for normality, will have

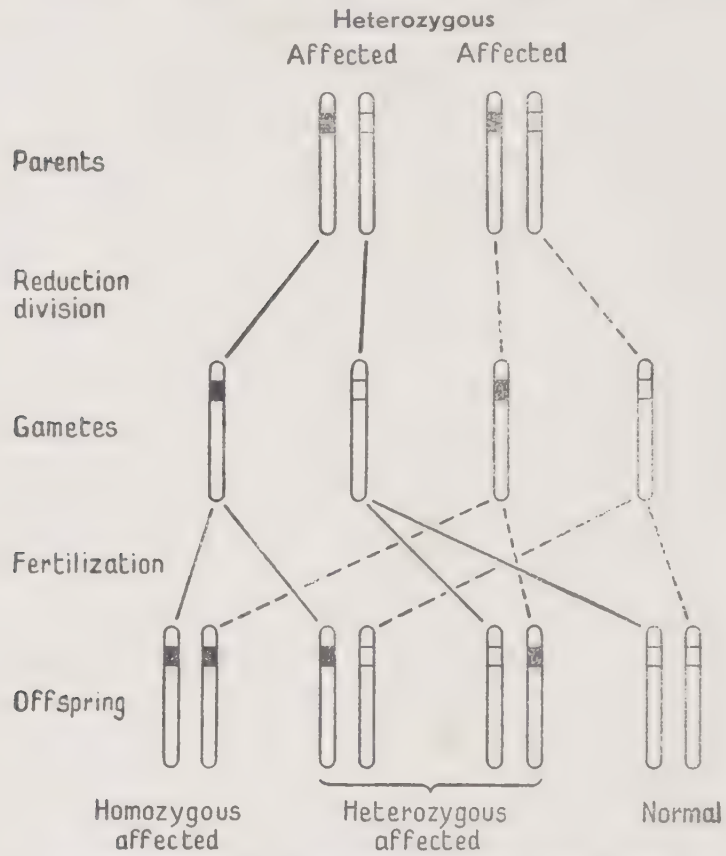


FIGURE 12 (*b*). GENES IN INHERITANCE

With both parents affected in one gene each, some children have both genes abnormal, in some neither are abnormal, and in some the condition is as in the parents, i.e., only one gene is abnormal. Where the abnormal gene is dominant both the parents and 75 per cent of the children must show the abnormality. Where it is recessive, the parents are clinically normal and 25 per cent of the children are affected.

two recessive genes. In the absence of a dominant gene for normality the abnormality becomes manifest. This explains the occurrence of some 'familial diseases'

or the appearance of several children in one family with the same disease, though the parents are outwardly healthy. That such familial diseases occur

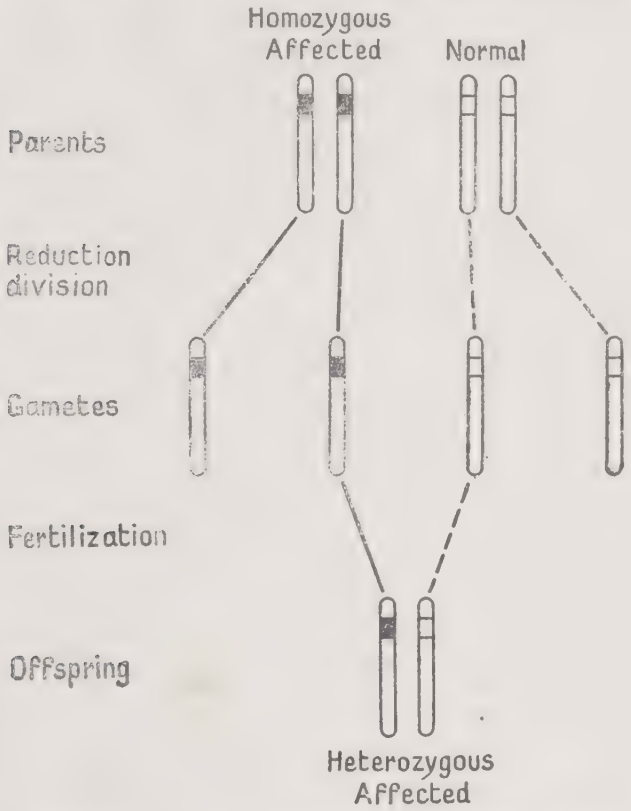


FIGURE 12 (*c*). GENES IN INHERITANCE

With one parent affected in both genes and the other in neither, all children must carry both an affected gene and a normal one. If the abnormal gene is dominant all children are clinically affected; if it is recessive all are clinically healthy. The affected parent is clinically abnormal whether the condition is dominant or recessive, as he has no gene for normality.

more frequently in cousin marriages or in highly inbred groups is explained by the fact that similar recessive genes are more likely to be carried

by related individuals than by individuals of different stock. This of course applies equally to desirable

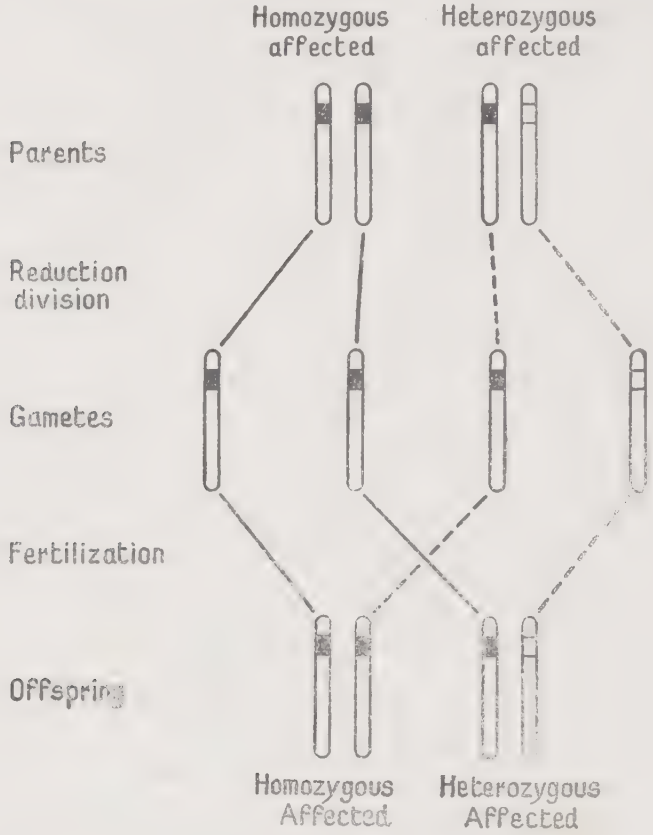


FIGURE 12 (*d*). GENES IN INHERITANCE

With one parent affected in both genes and the other in one only, all children must be affected genetically. If the condition is dominant both parents are affected clinically and all the children too. If the condition is recessive the heterozygously affected parent is clinically normal, and the 50 per cent of the children heterozygously affected are likewise clinically normal.

recessive features as to abnormalites, though undesirable variants from the normal are much more frequent.

In the case of dominant hereditary abnormalities, all children are bound to be affected if both genes in

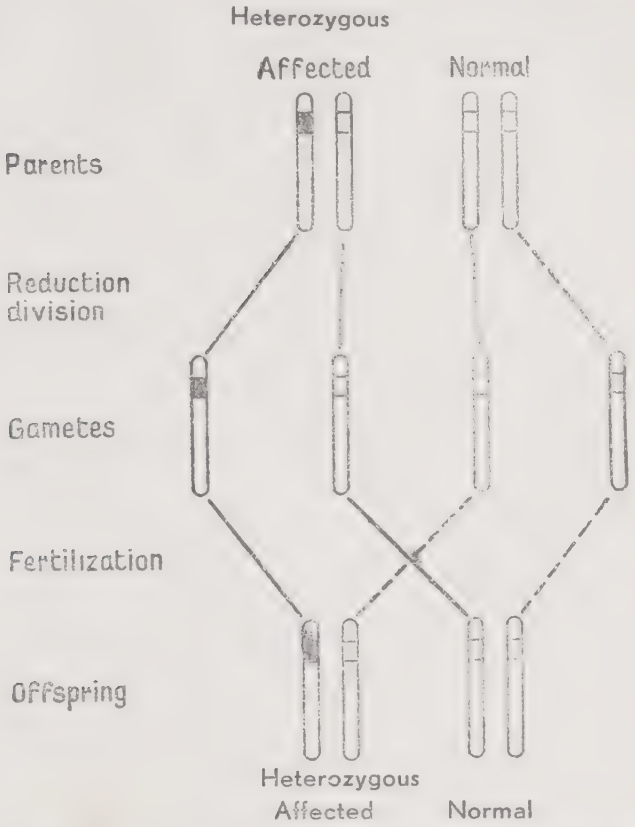


FIGURE 12 (*e*). GENES IN INHERITANCE

With one parent affected and only in one gene, 50 per cent of the children will likewise be affected. If the condition is recessive neither affected parent nor children are clinically diseased. It dominant, the heterozygous parent and heterozygous children are clinically affected.

(It should be understood that percentages refer to large statistical masses. In any particular family these strict mathematical relations are not to be expected.)

each parent or in one of them carry the abnormality. It will affect 75 per cent of the immediate progeny

if both parents are abnormal on one gene only, and 50 per cent if only one parent is abnormal, and the abnormality is carried by one gene. What is important in these considerations is the recognition that given an inherent abnormality in a gene, the basis for hereditary disease is established. The disease is transmitted from generation to generation when the

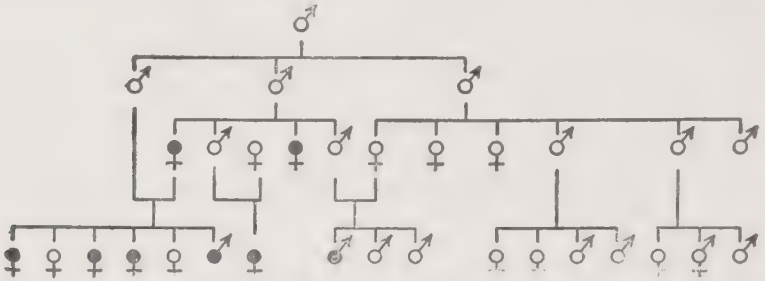


FIGURE 13. RECESSIVE INHERITANCE

Four generations shown. From the behaviour of the third and fourth generations it can be inferred that the first and second generations, though outwardly normal, were carriers and that the second members of the second and third generation married carriers. The affection transmitted was albinism.

Symbols used: ♂ = unaffected male.
♀ = unaffected female.
♂ = affected male.
♀ = affected female.

abnormal gene is dominant, while recessive disease becomes manifest only under certain genetic circumstances, when it appears as 'familial' conditions occurring in the offspring of clinically healthy parents.

3. Hereditary disease

Hereditary malformation and disease are not uncommon. Mental deficiency, deaf-mutism, and colour blindness are some common recessive hereditary

diseases, while dominant affections may range from such relatively innocuous conditions as stumpy fingers (brachydactily) to crippling defects like claw-hand and foot. The recognition of some 'familial diseases'

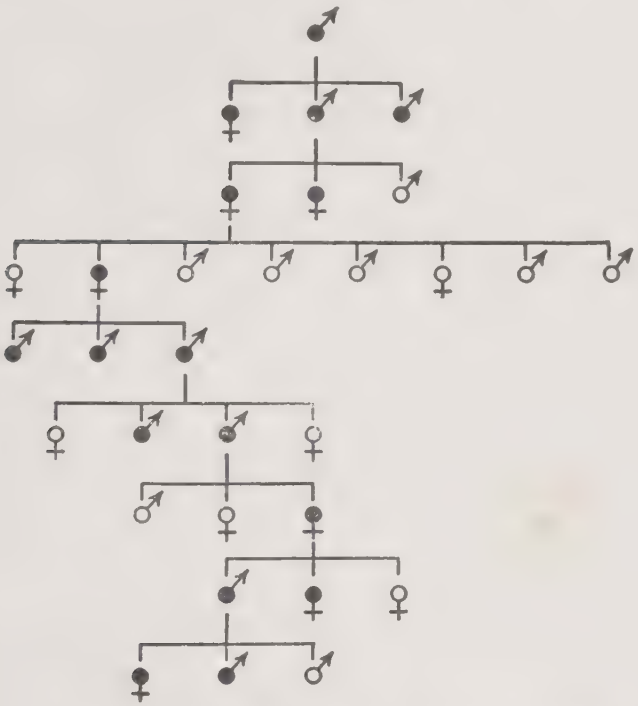


FIGURE 14. DOMINANT INHERITANCE

Part of the Nougaret genealogical tree traced back to 1637. Successive generations have been afflicted with night blindness.

Symbols used: As in Fig. 13.

as hereditary (recessive) in character has given a new orientation to the study of a vast group of anomalies to which no satisfactory approach was previously available.

The conception of abnormal genes as the basis of

disease carries several important implications. Recessive hereditary disease in man generally appears unexpectedly in a family, for it is caused by the unfortunate circumstance that both the parents carry the recessive factor, usually unbeknown to themselves (Fig. 13). Theoretically the elimination of dominant hereditary disease is simple enough—affected individuals need only abstain from raising families (Fig. 14). The elimination of recessive affections has as yet no easy theoretical possibilities, for only exceptionally has an individual a family pedigree sufficiently extensive to reveal the possibility that he is a carrier of a deleterious recessive factor. Moreover, most individuals do carry such factors. In the case of rare recessive affections the chances of meeting a mate in the general population, as distinct from one's own relations, who carries the same recessive factor are remote, but always existent.

Hereditary disease is largely a self-limiting process. Any disadvantageous factor militates against survival in the outer world, and still more against perpetuation. A more significant restriction arises from the fact that abnormal genetic characters are not isolated entities but part of the total genetic constitution of an individual. Genes have a modifying effect on each other, so that the manifestations of a particular gene may be suppressed (and this applies to abnormal genes as much as it does to genes carrying normal characters). Even dominant genes may be suppressed by the sum-total of gene action, as is seen in the

occasional 'skipping of a generation' in dominant affections. Further limitation of hereditary disease arises chiefly from another set of circumstances: an intensification of the abnormal character may render life impossible. Gross abnormalities in the gene are indeed lethal to the embryo; an intensification of a dominant anomaly by a double inheritance of an affected gene from each of the parents, and the juxtaposition of two recessive genes (each non-lethal by itself) are frequently rendered impossible from non-viability of the offspring : miscarriage or still-birth results. It is thus that the miscarriage rate among families with abnormal inheritance is explicable, and the explanation has been verified experimentally in animal breeding.

Moreover, some hereditary conditions affect the capacity to reproduce, sometimes biologically and frequently from social considerations involving both aesthetic and economic factors. Relatively innocuous hereditary anomalies like colour blindness have no such limitations, but there is no gross hereditary anomaly, whether dominant or recessive, that does not call into operation a complex series of biological and social factors that militate against its survival. That this process is, however, not absolute is seen from such exceptional conditions as Huntington's chorea, a dread hereditary palsy which makes its appearance late in life—after the reproductive age—leaving the carrier of the affection biologically and socially free to transmit it.

The gene has no self-sufficient existence. It is part and parcel of the changing stuff of the universe and is itself extremely unstable. Were genes rigid entities inherited mechanically over generations, evolution could only consist of an endless reshuffling of characters by the process of sexual reproduction, external conditions acting as selective agencies, favouring or eliminating certain combinations. Actually the gene is constantly undergoing explosive internal changes, giving rise to new characters. These are the 'mutations' of the biologist; they make possible an infinitely more varied evolution of life than could be given by natural selection operating on rigid hereditary material. Not all mutations are favourable; in fact most are unfavourable or at best neutral, and the problem of hereditary disease is but one aspect of this larger issue of mutations. Dominant and recessive gene anomalies are constantly arising spontaneously; most are probably of little significance individually and racially; many are incompatible with life, but 'new' hereditary diseases are part of the scheme of things, for 'new' mutations are the basic condition for evolutionary development. As opposed to the more or less feasible practical control of hereditary diseases, their complete elimination implies man's capacity to control not only life but the restlessness pervading the universe.

Hereditary diseases are not limited to disorders present at the birth of the child. An hereditary affection may be incompatible with the birth of a

living child, but it is also compatible with the birth of an apparently healthy child, the disorder becoming manifest at almost any period in life: in childhood as with amaurotic idiocy, after middle-life as with Huntington's chorea, or even in old age, as perhaps with 'senile' cataract. These hereditary affections setting in, not as malformations or disturbances present at birth, but at some later period in life, ranging from infancy to senility, are known as abiotrophies, the supposition being that the hereditary constitution of the affected tissues is such that they die before the other tissues of the body: a sort of localized hereditarily determined death which does not disrupt the life of the body as a whole. Many eye diseases, such as retinitis pigmentosa which sets in in childhood and leads to blindness, and many nervous disorders, such as the particular form of paralysis and lack of co-ordination known as Friedreich's ataxia, are abiotrophic in character. In contrast to the abiotrophies are the phakomatoses, a relatively rare group of hereditary affections. In the abiotrophies the individual is born 'perfect'. In phakomatoses minimal blemishes, like 'mother-spots' on the skin, are the starting point for hereditary diseases of a progressive character; as opposed to the disintegrative changes of slow localized death seen in the abiotrophies, the phakomatoses have some features in common with tumours.

The significance of heredity as a factor in disease has gained greatly from the realization that birth

is but a dramatic moment in the life of an individual, the prenatal and post-natal phases constituting one continuous event, which itself is only an infinitesimal part of racial life. From the point of view of the life of the race the individual body ('soma') is the husk that gives temporary shelter and a field of action to that tiny quantity of potentially immortal hereditary matter stored in the reproductive cells (Fig. 15).

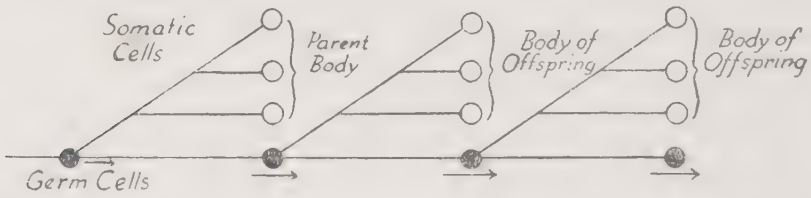


FIGURE 15. THE CONTINUITY OF GERM PLASM

The germ plasm (the reproductive material) is handed down from generation to generation; the body (the s o m a) is an incidental development and is discarded.

4. Acquired disease of ante-natal origin

The dampness and darkness of his mother's womb constitute man's first contact with a larger world, and the nine months of gestation are packed not only with the tremendous events of fertilization exploding a quiescent ovum into volcanic life, but also with the eventful story of the interaction of this developing life with its environment.

Increasing parental care marks the course of evolution. Fertilization in plants by wind-borne pollen, and exposure of the fertilized ovule to wind and air, the exposure of the fertilized fish ovum to the buffetings of the sea, gives way to the protection of the

fertilized bird ovum by a shell and the mother's care. This is carried still further in mammals, in whom the fertilized ovum is nurtured and nursed within the mother's body and the prolonged period of human gestation marks a high point in the protection of the future generation. Within the mother's womb the growing embryo is not exposed to fluctuating temperatures, extreme changes in environment, failure of nutrition, and the endless struggles against 'Nature red in tooth and claw'. The destined development of the ovum runs a smooth and placid course. This, however, may be disturbed drastically, as the womb does not supply complete isolation from the outer world and its irruptions. Such disturbances are the causes of one variety of congenital disease.

The growing embryo is nourished by the blood of the mother, and this blood is carefully filtered by the placenta—a sort of fleshy disc attaching the embryo to the womb. So effective is the placenta as a filter that but few noxious substances circulating in the blood-stream of the mother pass the placental barrier, and a sickly, ailing mother often gives birth to as healthy a child as is conceivable. The process of rearing this growing life within her may indeed kill the mother—as by kidney disease—and yet the noxious substances in her blood that kill her may never reach the embryo. But this placental barrier is not absolute, so that intra-uterine disease does occur. Syphilis is an important example : a syphilitic mother is unlikely to bear a healthy child. The mani-

festations of syphilis in the growing embryo are protean. There may be gross disturbances at an early stage leading to non-viability and consequent miscarriage, extensive lesions in a puny child born condemned to an early death, or an apparently healthy child, who, however, will develop syphilitic lesions later on. A considerable (but constantly decreasing) percentage of patients in institutions for cripples, mental defectives, the blind and decrepit are drawn from the ranks of congenital syphilitics. Severe disturbances in the offspring are also produced by such a mild disease in the mother as German measles affecting her early in pregnancy, whilst minor ravages may result from other maternal diseases that the placenta does not hold back.

The vulnerability of the growing foetus to these influences is part of its vulnerability to minimal disturbances in optimum conditions for its development—a vulnerability far greater than that of adult tissues. Experimentally, fertilized ova placed in nutrient media differing slightly from the normal (by deviations in the degree of alkalinity or in the quantity of essential elements or by the addition of foreign substances) develop into monstrosities (Fig. 16). The resultant changes are always more severe when the experiment is applied in the earlier phases of development. Thus the addition of a given amount of substances such as ether, alcohol, or various salts to the nutrient medium may give rise to a non-viable, double-headed monster at an early stage, defective

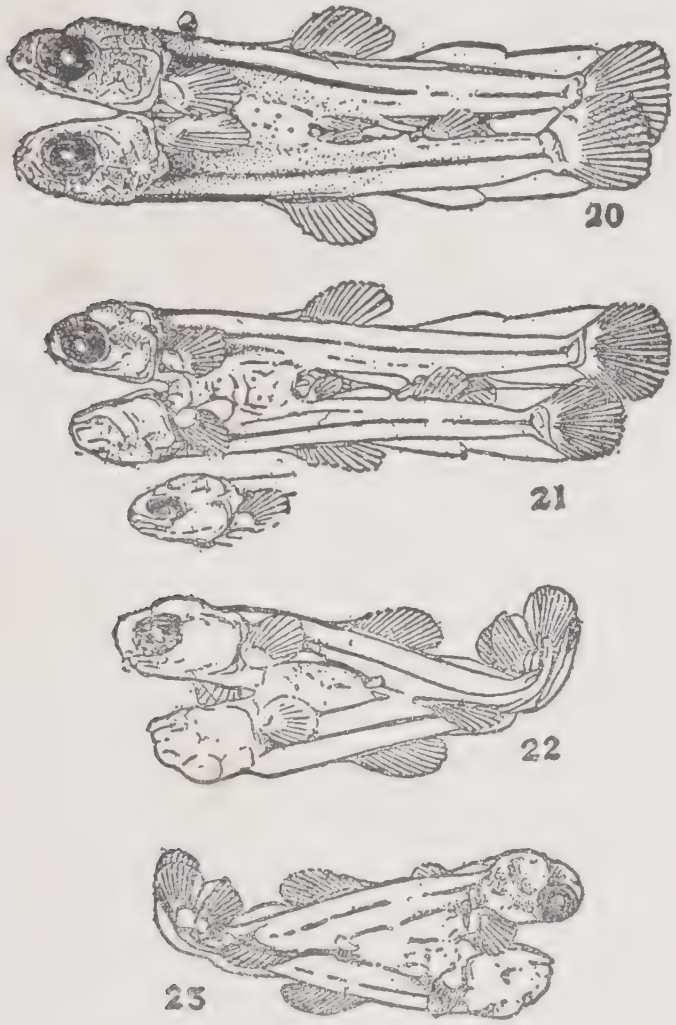


FIGURE 16. MONSTROSITIES CAUSED BY CHANGES IN THE ENVIRONMENT OF THE EMBRYO

Duplicate and twin formation in young fish induced through lack of oxygen at an early stage of embryonic life. Similar conditions have been induced in minnows by lowering the temperature of the egg during early stages.

development of the central nervous system at a later stage, and abnormal growth later still; in the newborn animal feeding with these substances may produce transient disturbances, and in the adult none at all.

The constitution of the mother is thus of the greatest importance to the developing embryo. The racial consequences of malnutrition during pregnancy are well recognized, and have an experimental counterpart in the observations that pregnant guinea-pigs on a controlled poor diet produce puny offspring. Pregnant sows deprived of vitamin A produce offspring lacking eyes. Generally speaking the human mother may be regarded as the food supply of the developing embryo and a deficiency or defect in that food supply is of serious consequence to her anthropophagous progeny.

The immediate environment within the womb, apart from the total of maternal influences, may also affect the developing embryo. The amniotic bag and its contained fluid form a sort of cushion supporting the embryo, and occasionally obscure changes within this fluid lead to the formation of bands. These may act as veritable surgical knives, for a band may constrict a growing limb to such an extent that the part below the band fails to develop and is actually shed, the child being born legless or armless. Occasionally the umbilical cord, which binds the foetus to the placenta, may act as a constricting rope extinguishing foetal life altogether.

It is difficult to assess the relative significance of

genetic factors and of disturbances in the environment of the growing embryo as causes of malformations and disease. In either case, extreme deviations are incompatible with life. The embryo's insistence on healthy parents is life's denial of the shabby and the second-rate.

5. The internal balance of the embryo

The embryo, which has thus far been regarded as hereditary material interacting with a sheltered environment, has a personality of its own no less than the adult. An internal balance of the developing embryonic organs to each other and to the entire embryo unfolds progressively with development, for with the growth of embryonic organs local conditions arise that influence development as a whole. Imbalance within the embryo produces profound effects—effects all the more readily excited in view of the great vulnerability of the growing embryo to departures from optimum conditions. There is some evidence that the development of the brain is hindered by abnormal development of the suprarenal gland. The internal disharmonies of the developing foetus are, however, a field of study that as yet has been scarcely explored. Racial and parental inheritance, maternal environment—and through it the outer world—and the internal balance of the embryo, all contribute towards the creation of that balance or imbalance of forces that constitutes the well-formed or ill-formed body, destined to serve as the temporary receptacle of an instant of Life.

CHAPTER IV

Disease: The Ill-Balanced Body

1. The endocrine system

Beginning with an isolated observation in 1786, there came to be recognized during the first half of the nineteenth century a condition now known as Graves' disease and by a number of other names. It presents a striking picture. The patient, generally a woman, is highly strung, the eyeballs are prominent, there is some swelling of the neck, the skin is moist and flushed, the outstretched hand shows marked trembling of the fingers, and a rapid pulse is present. It is a picture of life at an intense pitch—the candle burning at both ends. In the multitude of symptoms the enlargement of the thyroid gland to which the swelling of the neck was due did not first attract attention as a causal factor.

As the nineteenth century proceeded other conditions with a multitude of symptoms and the involvement of apparently functionless organs—as the thyroid gland, among others, was held to be—came to be recognized. In Addison's disease there was bron-

zing of the skin, extreme weakness, and destruction of the suprarenal glands, while the thyroid gland was found implicated in several disturbances. In myxoedema the patient looked heavy, lethargic, and bloated; the disease was recognized as similar to the symptoms sometimes observable after operations for goitre, and to cretinism in children, in whom the same heavy, lethargic, bloated appearance was present in addition to gross mental and physical backwardness. It was surmised that in these three conditions the essential feature was failure, removal, or congenital absence of the thyroid gland—a contrast to Graves' disease, in which the gland was enlarged and over-active.

These observations led slowly to the recognition of organs in the body which had important functions, though the organs seemed self-contained, having no ducts to lead away the products of their activities. It was thus that the conception of internal secretions or hormones from ductless glands was evolved : these organs produced substances that passed directly into the blood-stream. A number of ductless glands are recognized and different clinical pictures have been correlated with morbid changes in one or other of these glands. The tempting suggestion that disease only supervenes when these glands produce perverse or abnormal secretions has given way to the recognition that a series of disorders are the result of excess or lack of normal internal secretions and that these normal secretions are essential for the maintenance of health and life itself.

The recognition that excess of thyroid secretion leads to the hectic living of Graves' disease, and diminution of it to the vegetative existence of myxoedema and cretinism, led to the finding that a wide range of bizarre manifestations could be linked up with changes in the pituitary gland, a small organ less than half a gramme in weight, highly protected in a bony shelter at the base of the brain. These changes are not just one aspect of the general picture, but their immediate exciting cause. The striking clinical picture of gigantism—the overgrown, feeble giants of the fun fairs—was found to be correlated with morbid changes in the anterior part of the pituitary body (overaction of the eosinophile-staining cells), and could be reproduced in dogs by injections of suitably prepared extracts of the gland. Similarly, some dwarfs have underactive pituitary bodies, and extirpation of the anterior part of the pituitary gland in the puppy produces dwarfism. The production by the pituitary of a growth hormone was thus established, and a variety of clinical pictures were recognized as the result of disturbances in its functioning, the age at onset being important. Should the pituitary become overactive before growth is completed, gigantism results; after completion of growth pituitary overactivity shows itself in the coarsening of features and enlargement of hands and feet seen in acromegaly. In fact acromegaly and gigantism are fundamentally the same disturbance, producing dissimilar results owing

to the difference in plasticity of the material upon which the growth hormone operates. Similarly, pituitary underactivity produces dwarfism and feebleness in the young and a severe wasting disease (Simmonds' disease) in the adult.

The significance of these and similar observations lies in the fact that a whole range of 'diseases' were now seen as disturbances in the normal balance of the body. Rational treatment therefore aims at restoring the balance, and striking successes have attended several theoretically derived procedures: myxoedema and cretinism respond to thyroid feeding; Addison's disease, which was previously rapidly fatal, is controlled by extracts of the outer layers (cortex) of the suprarenal glands, and diabetes by insulin, which is the internal secretion of the pancreas.

2. Its integration

A number of hormones have been isolated and chemically synthesized in the laboratory, but the complexities of the problem of internal body balance arise from the fact that the elaboration of hormones is not confined to the limited number of ductless glands in the body, and that their effects are not simple but highly interactive. An internal secretion of great importance (insulin) is liberated by the pancreas, which is a double organ in that it also produces an 'external' secretion in the form of pancreatic juice, which is led by a duct to the small intestine (duodenum) to assist the process of digestion.

The duodenum itself produces an internal secretion (secretin) which stimulates the production of pancreatic juice, and this is but one example of the interaction between internal and external secretory organs. Most tissues in the body contribute substances that help to maintain the internal balance, and the ductless glands must be regarded not as something distinct, but as the most specialized organs of a generalized function.

That generalized function is neither simple nor autonomic to any extent. Graves' disease is the relatively simple response to excess of thyroid hormone, as myxoedema is its counterpart, but in a variety of disturbances it is difficult to implicate any particular ductless gland as the cause. Thus the rare condition of progeria in which a child looks like a very old person, may occur with disturbances of either the pituitary or the suprarenal gland. Similarly either of these or both may be affected in Cushing's syndrome in which there is obesity, purpling of the skin, raised blood-pressure, and considerable sexual abnormalities that in women (in whom the condition is commonest) take the form of development of masculine features (virilism). The fact that in many syndromes due to disturbances in the ductless glands diabetes and sexual abnormalities frequently occur, indicates still further that a clear-cut effect of excess or diminution of a particular hormone is the exeption. Once the balance is disturbed in one direction, a series of secondary disturbances set in. A considerable

degree of central control is, however, exercised by the pituitary gland.

The pituitary gland is itself a highly integrated organ. From studies ranging over anatomy, embryology, comparative physiology, experimental investigations, clinical medicine, and post-mortem appearances, the pituitary is recognized as consisting of three distinct parts, each with its own set of functions. The growth hormone is produced in the anterior part, from cells that stain with eosin (eosinophile cells), but cells staining with basic dyes (basophile cells) are also present and produce a different hormone, which affects, if it does not completely control, the sex glands and sexual activity. Indeed it is held that the balance between eosinophile cells and basophile cells is such that the predominance of the first determines growth in the sexually immature child, and that puberty is the manifestation of the shifting of the balance in favour of the basophile cells. There is certainly a definite antagonism between the secretions of these two types of cells, for experimentally the clear-cut results of an injection of basophile hormone is neutralized by a simultaneous injection of eosinophile hormone. Minor degrees of sexual abnormalities are regarded by some as a simple expression of minor derangement of the basophile action, and in Cushing's syndrome, with its fatal course, there is marked hyperactivity of the basophile cells (Basophilism).

The integrative action of the pituitary gland on the other ductless glands is such that it has been designa-

ted as the leader of the endocrine orchestra (Fig. 17), and diseases with symptoms suggestive of involvement of more than one gland (polyglandular disturbances) are regarded as pituitary disturbances primarily.

The control of the thyroid gland by the pituitary is shown by the fact that reduced thyroid activity occurs when the pituitary is affected or experimentally extirpated; injections of anterior pituitary extract restore the balance. Moreover, such injections in the normal animal produce symptoms of thyroid overactivity, though not the whole picture of Graves' disease.

The interaction of the pituitary with the pancreas is shown by the experimental observation that while removal of the pancreas causes diabetes from loss of pancreatic hormone (insulin), no such effect follows in animals whose pituitary has previously been extirpated; in such artificially stabilized animals (i.e. stabilized as regards the non-appearance of diabetes, but otherwise very much unstabilized) the injection of the missing pituitary hormone brings on diabetes. In fact the concentration of sugar in the blood at an optimum level is controlled by a complicated integrative process in which ductless glands and nervous system interact: there is a balance between a mechanism that tends to raise the blood-sugar and another that lowers it, the mechanism for raising the blood-sugar being largely controlled by the pituitary, directly and indirectly.

Interaction between the pituitary and suprarenal glands is seen from the fact that in progeria and in

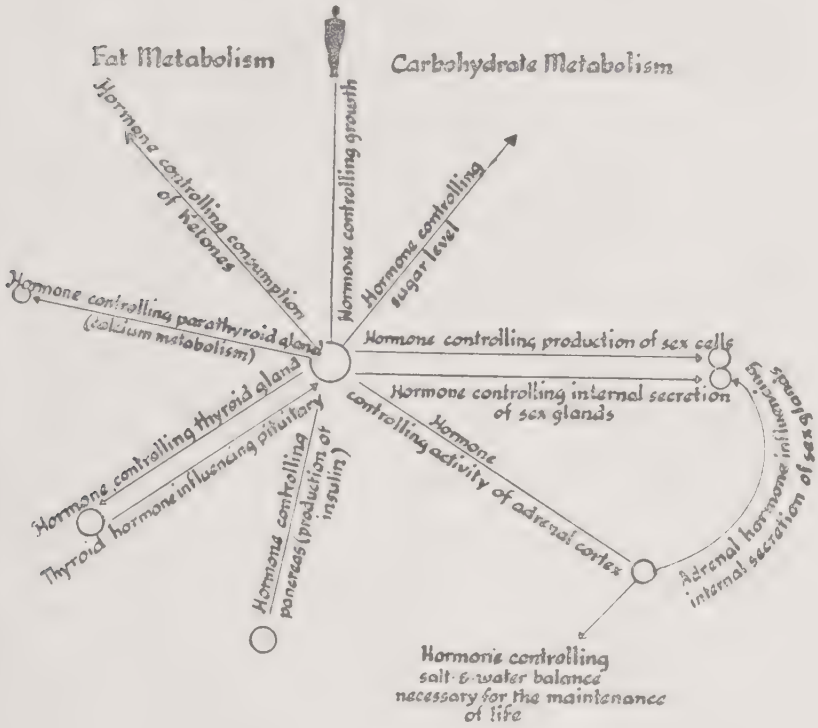

Fat Metabolism
Carbohydrate Metabolism
Hormone controlling growth
Hormone controlling consumption of ketones
Hormone controlling sugar level
Hormone controlling parathyroid gland (Calcium metabolism)
Hormone controlling production of sex cells
Hormone controlling internal secretion of sex glands
Hormone controlling thyroid gland
Thyroid hormone influencing pituitary
Hormone controlling pancreas (production of insulin)
Hormone controlling activity of adrenal cortex
Adrenal hormone influencing internal secretion of sex glands
Hormone controlling salt & water balance necessary for the maintenance of life

FIGURE 17. ACTION AND INTERACTION OF DUCTLESS GLANDS

The pituitary gland exerts a controlling action on other ductless glands and on some of the basic activities of the body.

The circle in the centre represents the pituitary gland. The smaller outlying circles stand for some of the other ductless glands.

Cushing's syndrome the suprarenal gland rather than the pituitary may be affected, and the dominance of the pituitary body is revealed by the experimental observation that anterior pituitary extracts induce

overaction of the suprarenal gland. Further evidence of integration is shown by the presence of sexual abnormalities in both pituitary and suprerenal tumours.

The pituitary has a direct controlling effect on sexual function. Extirpation of the pituitary in the immature animal will prevent sexual maturation, while injection of anterior pituitary extract causes enormously increased ovulation (ripening of ova). In the sexually immature female animal pituitary extracts induce maturation, while there is complete loss of sexual activity on extirpation or disease of the pituitary. The ovaries and testes produce, of course, hormones of their own, as is shown by the striking changes in the castrated or ovariectomized animals and by human eunuchs, but it is the pituitary which largely controls maturation and the cyclical character of sex-function. The hormones of both testes and ovary have been isolated and are chemically closely related (testosterone and oestrone), and there is some evidence that sex itself is largely a matter of the relative balance of these hormones. Both the hormones are found after puberty in the urine in the two sexes, in amounts not greatly dissimilar (though the amount excreted by the body is no indication of the amount used). 'Male' hormone is found in considerable excess over the normal in women with Cushing's syndrome, and 'female' hormone in men thus afflicted. It is suggested that the ovary is potentially a bisexual organ, with a feminine cortex (outer layers) and a rudimen-

tary masculine medulla (core), and that in diseases like Cushing's syndrome masculinization in women and feminization in men occurs from precipitating the heterosexual tendency present in all individuals.

The balance of the endocrine system is not a self-maintained system. The pituitary body is anatomically continuous with the diencephalon, the oldest part of the brain, which subserves such primitive instincts as hunger, thirst, sleep, and sexual activity. Physiologically, too, there is close interaction between the diencephalon and the pituitary; an injection of pituitary extract may sometimes overcome a cow's refusal to yield her milk for such psychological (diencephalic) reasons as objection to an individual dairyman or because the calf has been taken away. Graves' disease is frequently precipitated by a strong emotional experience and is more frequent at times of stress and hardship. While the significance of disintegration within the endocrine system in the production of disease is clearly appreciated, there is as yet but little understanding of the interaction of the endocrine system with that other great integrating agency of the body, the nervous system. That the interaction is considerable is obvious from the fact that the medulla of the suprarenal gland and the posterior pituitary are under full nervous control.

3. The integrative action of the nervous system

The nervous system serves to balance a constant stream of exciting and inhibitory stimuli. Part of the

mechanism is autonomic, i.e. it is performed without consciousness, and is carried out by the oldest part of the brain and nervous tissue in the body (the subcortical centres, the sympathetic and parasympathetic system).

Structural or functional imbalance of the sympathetic-parasympathetic system leads to such affections as Hirschsprung's disease, in which the colon becomes enormously enlarged owing to its incapacity to empty itself regularly, and to other disorders involving various sphincters of the body. High blood-pressure in some patients is perhaps also an expression of this overaction of the sympathetic nerve supply of the blood-vessels.

Imbalance in the mechanism of conscious nervous control may arise from anatomical defects in the pathways of nervous control, consequent on congenital or abiotrophic defects or on violence to the tissue from external injury or damage from internal causes. Disease arises from any failure to balance the endless stimuli that reach the brain.

4. The integrated cell

The balanced integrating action of the endocrines and the nervous system reveal how the body is marshalled to order in health and how a failure in that integration leads to disease, but the orderly or disorderly conduct of the body as a whole in response to endocrine or nervous stimuli is built up from the infinite local responses of cells to the stimuli that

reach them. This raises the fundamental problem of why one cell or group of cells is stimulated to activity by the same substance that depresses the action of other cells. Not all people respond to thyroid medication by increased activity; stimulating the vagus nerve slows down the inherent rhythm of the heart but accelerates that of the intestines. Again the response of a cell to the same stimulus is not always the same—the hormones that excite the sexual cycle in the female reproductive organs still reach them after the menopause, but the effect previously produced is now lacking. Such facts show that in the ultimate synthesis the stimulus is only one aspect of the complete effect, the response of the cell to the stimulus being the other. Neither exists independently.

Recognition that the cell has a balanced life of its own is of relatively recent date. To synthesize chemically even the less complex of proteins, lipoids, and hydrocarbons of the cell is often impossible without using high temperatures, sometimes several hundred degrees, yet the living cell is constantly building them at body temperature through the agency of a complicated co-ordinating system of intracellular enzymes (organic catalysts). A cell may behave abnormally from inherent defects no less than from faulty stimuli reaching it, though it must be appreciated that abnormal behaviour of a cell implies abnormality in relation to the integrated body of which it forms a part, but not necessarily to itself.

5. Disturbed cellular balance

Abnormal cellular response probably underlies two such markedly different groups of disorders as allergic diseases and cancer.

(a) The allergic diseases

The allergic diseases constitute a wide group of affections, of which asthma, hay-fever, migraine, and urticaria are outstanding examples. There is a strong hereditary tendency in these affections, and different members of a family may show different manifestations of the allergic state : one may be suffering from asthma and another from migraine. The disease in such patients is the manifestation of an abnormal response to a stimulus that excites no response at all in the normal individual. This explains the periodic character of allergic outbursts : hay-fever in the affected individual comes only on exposure to particular pollens present at a particular time of the year only; eczema may be excited by a particular food. The significant thing is that the patient reacts abnormally in what must be regarded as a normal environment.

That the abnormal response lies in the cell itself is suggested by the observation that if isolated tissue like intestine or uterus, suitably prepared (by generalized sensitization), is suspended in a nutrient medium it reacts explosively to the addition of a minute quantity of the sensitizing agent (Dale-Schultz phenomenon); furthermore, locally sensitized tissue in the intact animal reacts similarly on the

addition of the sensitizing substance to the blood-stream (Schwartzman phenomenon). It is surmised that a disturbance in the balance within the cell is responsible for its inability to react normally to a common and generally innocuous stimulus.

If the allergic diseases are a manifestation of inherent instability of the cell in relation to the integrated function of the body as a whole, cancer may similarly be regarded as the response of an isolated cell growing without regard to the balance of the body as a whole. Cancer tissue is intensely alive and functioning; it is malignant in relation to the body economy, but not to itself.

(b) Cancer

The synonyms cancer and malignant disease indicate two essential features of the affection : the crab-like creeping infiltration into normal tissue by the cancerous growth and its lethal character to the body as a whole. All cancers probably start in one cell only, but the increasing growth, the spread into adjacent tissues and the dissemination by the blood-stream to distant parts of the body, where imported cancer cells develop into independent growths (secondary deposits) soon lead to mechanical interference with the normal body functions. Thus a growth in the oesophagus prevents food from reaching the stomach; a secondary deposit in the brain kills by compressing vital centres. Less defined factors that contribute to the death of the patient are septic complications from ulcerated cancerous lesions, lowered general health

and its complications, and perhaps also a toxic state produced by the cancer tissue. The individual cancer cell differs little in structure from the normal cell; often no difference at all can be established by the microscope, though the relation of the cells to each other and to the normal tissue is characteristic. Yet the cancer cell leads a different life from the normal cell; for its energy requirements it is capable of breaking down sugar in the absence of oxygen, which is essential to the normal cell (anaerobic glycolysis against aerobic glycolysis). The cancer cell is so active that it can break down its own weight of sugar in ten hours, and though normal embryonic tissues share with cancer a capacity for anaerobic glycolysis they can only achieve it to a much smaller extent. The cancer cell contains a factor that promotes growth, as can be seen from the fact that an extract of cancer tissue added to normal isolated cells in culture media stimulates growth to such an extent that the process may become continuous and automatic. But the cancer cell also contains a factor inhibiting growth; the outbreak of cancer and the different degrees of growth capacity (and therefore severity of the disease) are probably determined by the degree of dominance of the growth factor in the cancer cell over the inhibiting factor. Inhibitors are probably widely present in tissues; they have been extracted from cow's placenta to check the growth of transplanted cancer tissue.

Once the cancer process has started it continues even if the stimulus exciting it is removed. Repeated

painting of the skin of a mouse with certain coal tars (benzanthracene compounds) induces after a time cancer at the site of painting; if the painted skin is transplanted to another mouse before cancerous changes develop, cancer will develop in the transplant though the stimulus is absent and the host is different. What starts the cancerous process in the cell is unknown. Experimentally a number of possible stimuli have been established : parasites (nematode worms) excite cancer of the stomach in the rat, filter-passing viruses cause growths in fowls, and many coal-tar derivatives painted locally on to the skin or injected into the blood-stream excite characteristic tumours. Most of these factors are not normally present in the body, but considerable importance attaches to the coal-tar derivatives, for cancer-producing coal-tars fall in the sterol group of chemicals, and are closely related to bile acids, cholesterol, and vitamin D, which are normal products of the body, and to oestrin, the normal internal secretion of the ovary. The link extends still further, for in the embryo development commencing in one particular area determines the orderly sequence of further development. If that area be excised and transplanted elsewhere on to the embryo, a second orderly sequence of development is initiated at the new site. This area is called an organizer, and it exerts its organizing function chemically, for an extract of this organizer tissue ground up is as effective as the tissue itself. This extract is chemically

also a sterol. It would, therefore, appear that the chemical stimulus that organizes the growth of the embryo, the stimulus that determines the reproductive cycle with its active growth of tissue (as in menstruation), the vitamin that markedly influences growth of the child, and the experimental cancer producing coal-tar derivatives have not only some similarity in action but also in chemical composition. The fact that these sterols are again closely related to such common products of normal body function as the bile salts may also be significant as a possible cause of cancer-producing substances being liberated by the body itself under abnormal conditions. (Fig. 18). Moreover there is some experimental evidence that benzene extracts of human liver induces cancer in mice.

It must, however, be appreciated that the stimulus by itself is not cancer—or any other disease. The importance of the cell response to the stimulus is brought out by the clinical and experimental facts that heredity is a significant factor in cancer and that there is a marked organ-specificity in the sense that only certain organs will respond to a particular stimulus. Experimentally it is possible to breed a strain of mice that are highly resistant or highly susceptible to cancer—and to particular forms of it. Clinically 'cancer families' are known and the same organ is affected repeatedly within the particular family and frequently at the same age. The importance of the cell response to the stimulus is further

emphasized by the fact that the experimental production of cancer depends upon the animal used.

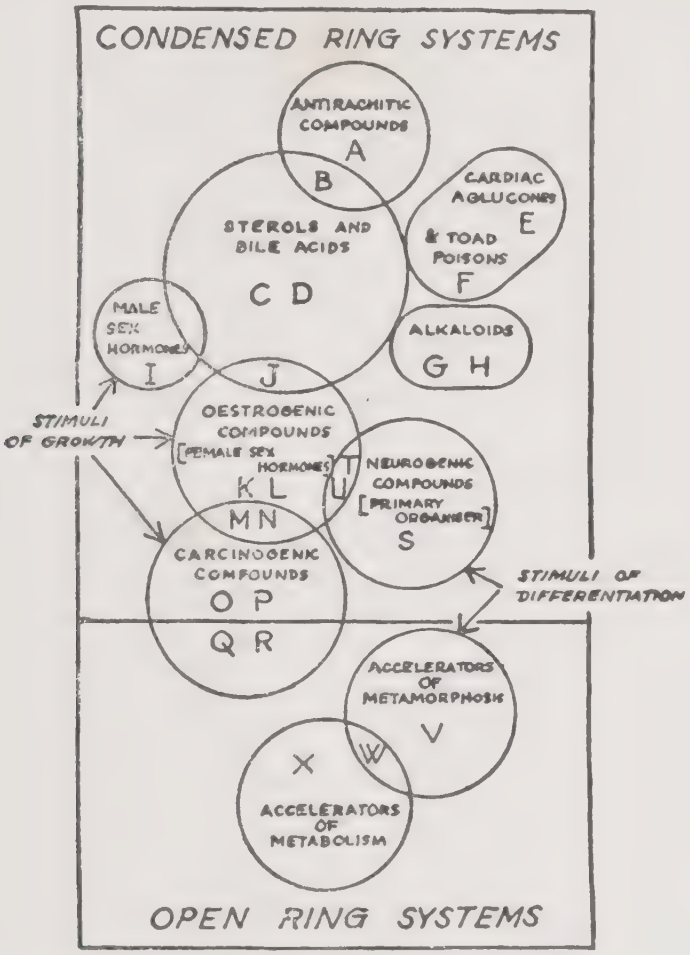


FIGURE 18. STEROLS IN LIFE

There is a close chemical relationship between embryonic organizers, sex hormones, cancer-producing coal-tars, growth-inducing substances, normal bile salts and some therapeutic drugs. All these substances belong to the sterol group.

Coal-tar produces cancer in the mouse and the rabbit, and in man, but not in the rat, dog, or guinea-pig,

while viruses are effective in the fowl and rabbit but not in other animals.

Cancer in all probability is the response of the cell to one of a number of stimuli, any one of which is cancer-producing. Once an ill-balance within the cell has been precipitated a self-geared process commences and runs its own course. During that course a number of events occur. Immunity against a second cancer is one of them. In an area of skin painted with coal-tar one spot only will become cancerous (and invade the rest of the tissue). Once a tar cancer has developed it is impossible to induce a second tumour by tarring, nor is it possible to induce tar cancer in an animal spontaneously diseased. It is this mechanism which explains why in spite of the much greater frequency of cancer of the reproductive organs in women, the total incidence of cancer in them is no more than in men; the other organs are immune to cancer. It is also this immunity which explains why in spite of a markedly different incidence of cancer of the various organs in Jews as compared to gentiles, the total incidence is the same in both groups.

The production of experimental cancer by both coal-tar derivatives and viruses may indicate the multiplicity of agencies that can induce a cell disturbance leading to cancer, but it is also possible that some unifying factor may underlie the various stimuli. Viruses, are on the borderline between the inanimate and the lowest forms of life. There is evidence that

they are self-multiplying enzymes rather than living particulate matter and some, at any rate, are crystalline in character. The gulf between the animate and inanimate is narrowed and it is perhaps not a fundamental issue whether the immediate exciting factor or factors of cancer belong to the totally inanimate or to the semi-animate. The more significant problem is whether the possible multiple factors can be reduced to one. The experimental observation that a rabbit treated with both cancer-producing coal-tars and cancer-producing viruses, reacts by a more active cancerous growth, does not necessarily indicate that these two cancer-producing agents are unrelated substances, for the combined effect of allied substances is often greater than that which is to be expected from a purely arithmetical addition (synergism).

CHAPTER V

Disease: The Abused Body

1. Not by bread alone

To the new-born child the first adventure in living is the exchange of a world in which everything conspired to keep him alive for one which ruthlessly tests his capacity to live. The embryo lives on its mother, and in a modified form this parasitical existence continues for some months after birth. His mother's blood and milk are man's sources of food for only a strictly limited time, after which he must wrest his sustenance from nature. In this struggle his capacity to live is often vitiated by the abuses he inflicts on his body.

The living organism is machine-like in its need for fuel to supply energy for the performance of its functions, but it also utilizes fuel for functions alien to a machine: growth, automatic replacement of wear and tear, and reproduction The fuel of a machine need only be calculated in terms of energy; man's food must supply not only energy, but also the material for growth and for incorporation into the ever-renewing living body. A diet that satisfies the needs of the body gives that harmonious relationship that signifies

health; one that only partially satisfies the bodily needs disturbs the proper functioning of the organism. Nutrition is thus a factor making for health or for disease.

Man does not make his food. His food consists of living or previously alive vegetable and animal matter. He himself cannot build living tissue out of inorganic matter as plants do, and in the final analysis he subsists on plants either directly or indirectly in so far as the animals he eats are also built up by plants. Man is a parasite on plants and the history of parasitism is an essential part of the history of civilization.

For millennia man's humanoid ancestors and primitive man himself were food-gatherers rather than food-producers. Man collected what he could find at hand—a process that left primitive man no option other than being a hunter. His food, and therefore his mode of life and mental processes, were determined by this overruling condition. His prey was mobile and there could be nothing but a nomad existence for him. Changes in weather, the endless migrations of his animal prey, and the absence of any bond to the soil made man a predatory rover. His food supply was never certain and often intermittent. The beginnings of agriculture were probably accidental in the Nile valley, where a natural crop of barley was made possible by the overflowing of the river. The imitation by man of this accident of Nature and the urgent need for storing animal food by capturing,

preserving, and breeding animals led to the greatest revolution in history. Man became a food producer. Nomadic life was abandoned and there emerged the settled community with its specialization, co-ordination, customs, and traditions. Civilization had begun.

The development of agriculture is a constantly unfolding process, as fluid to-day as it was in the beginning. Purposive effort can create 'new' types of plant and animal life, as the activities of agriculturists and stock-breeders show. The transplantation of the potato into Europe illustrates one of the far-reaching effects of conscious effort, just as the 'creation' of new types of corn and of such produce as the grapefruit illustrates the endless possibilities of deliberate search for an ever wider range of foods.

The variety of food in a community depends on the soil, climate, and the particular stage of technical development, modified by such factors as custom and social needs. Hence the range of dietary habits of different countries and different sections of the community. These various dietaries all sustain life, for otherwise there would be no communities to perpetuate their existence. They are, however, not all equally satisfactory for the purpose of well-being as opposed to mere existence.

2. Field observations on diets

India, with its enormous expanse of territory and its teeming millions with their great diversity of

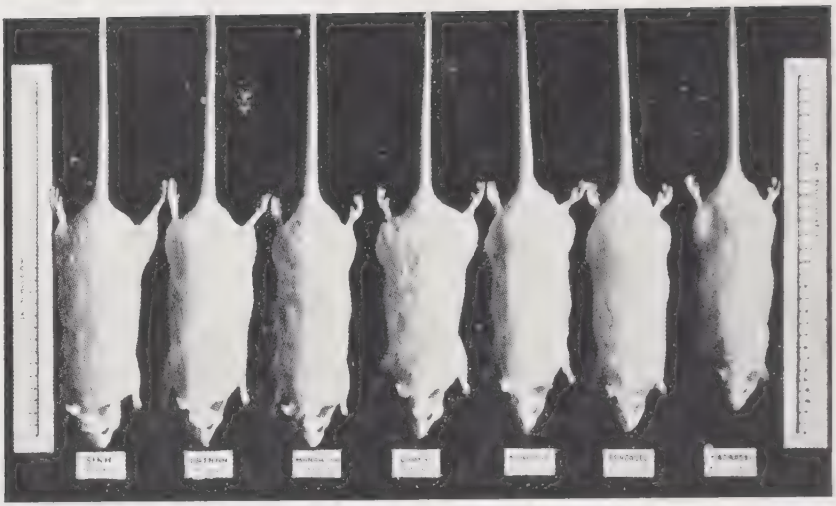


Fig. A. DIET AND PHYSIQUE

Representatives of seven groups of rats fed from the same early age on certain national diets of India. The Sikh diet (extreme left) is rich and varied; the Madras diet (extreme right) is composed mainly of rice.

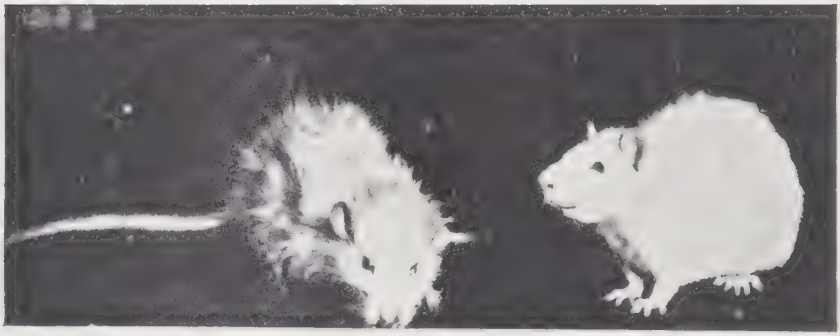


Fig. B. PROLONGATION OF YOUTH AND LIFE

The old rat on the left is the last survivor of a normal group. The 'young' one on the right is the same age, maturity and senility having been delayed by a controlled diet, preventing growth and development.

customs, has been the centre of much field-work on the value of different diets. Generally speaking, the health and physique of the northern races in India is better than those of other Indian races. A number of factors may enter into the great range of physique (which is excellent in the Punjab, and declines steadily towards the south, the poorest level being reached in Bengal and Madras), but laboratory experiments show the predominant significance of diet. Rats fed on standardized diets corresponding to that of seven Indian groups showed variations in physical development closely parallel to those observed in the Indian population : at the end of six months (corresponding to sixteen years of human life) the average weight of rats fed on the Sikh (Punjab) diet—rich in whole wheat, milk, and vegetables—was 235 grammes, that of rats fed on the Madras diet 155 grammes, and the other regional dietaries gave intermediate figures (Fig. 19). Food of the type consumed by the poor populations in Europe also compares unfavourably with the Sikh diet (Plate I, Fig. A). In contrast to the rats fed on a Sikh diet, those fed on a poor European diet did not increase in weight, showed stunted growth, were badly proportioned, had coats lacking gloss, were nervous and spiteful to their attendants, and formed an ill-disposed community, the stronger killing and eating the weaker ones. The incidence of disease was markedly greater in the group on a poor European diet and in another on the Madras diet than in a group on the Sikh diet; there was more

polyneuritis, gastro-intestinal disturbances, and pulmonary disease—a point of significance, as both pulmonary and gastro-intestinal diseases account for a great proportion of sickness both in Madras and in Europe (Fig. 20). By changes in diet many diseases could be produced. Some like gastric ulcer and stone in

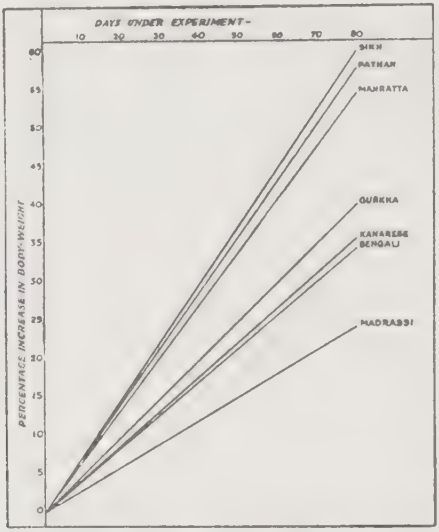


FIGURE 19. DIET AND PHYSIQUE

Graphic representation of the findings in an experiment on seven groups of rats fed from the same early age on certain national diets of India. The Sikh diet is rich and varied; the Madras diet is composed mainly of rice.

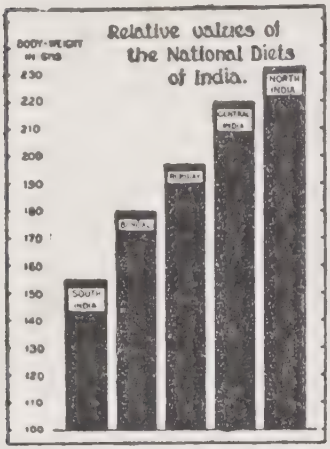
the kidney, are apparently direct consequences, others, like pneumonia and a series of other infections, arise indirectly from preparing the soil on which infection can operate. The health-giving Sikh diet is easily disturbed; if milk is excluded and fresh vegetable foods limited, degenerative changes in the mucous membranes of the body appear, with consequent development of respiratory and gastro-intestinal diseases.

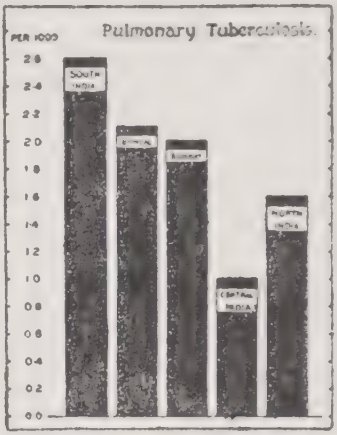
Experience in India is supported by observations elsewhere. The pastoral Masai tribe in East Africa live largely on milk, meat, and blood; their fine physique and health contrast strongly with the poor physique of the adjacent agriculturist Kikuyu tribe, who subsist on the usual cereal and vegetable diet common in Africa and Asia. Striking improvement in the physique of children of Japanese and Chinese settled in the U.S.A., with its high standards of nutrition, are ascribed largely to the dietetic improvements, while the Japanese in their homeland were steadily increasing in size as standards of living and diet improved. The addition of generous quantities of milk to school diets is amply justified by the controlled observations carried out in many countries.

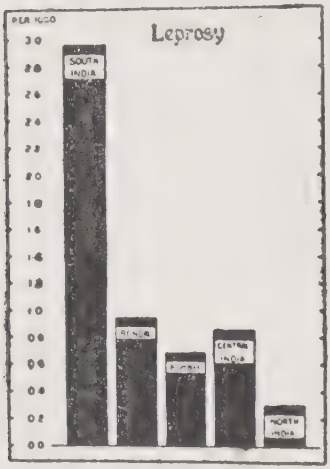
3. Empiricism in dietetics

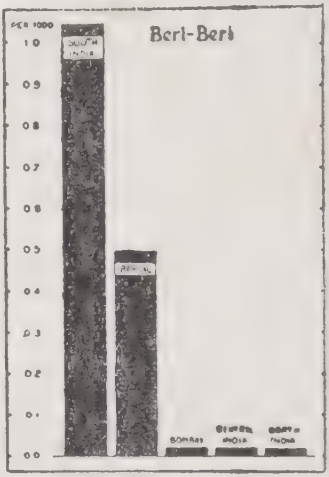
Throughout the centuries man has groped his way towards a satisfactory diet, but only calamities could disclose to him the imperfections and defects of his staple foods. Scurvy was an ever-present menace to sailors on the seas, and the recognition that fresh fruit was an essential constituent of the diet if this scourge was to be overcome came slowly. More frequently the elimination of disease due to food deficiencies came indirectly with changes in the diet. Medieval records show a great prevalence of stone in the bladder, now a relatively rare condition. Its disappearance was not altogether due to the development of more balanced diets, for the coincidental

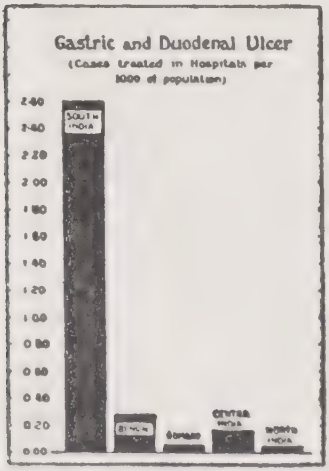
NUTRITIVE VALUES OF DIETS IN COMMON USE IN THE FIVE MAIN DIVISIONS OF INDIA, AS DETERMINED BY FEEDING EXPERIMENTS ON RATS, COMPARED WITH THE FREQUENCY DISTRIBUTION OF CERTAIN DISEASES PER 1000 OF SICK PERSONS IN THESE DIVISIONS.











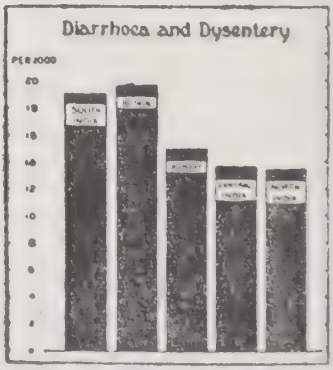


FIGURE 20. DIET AND THE INCIDENCE OF SOME DISEASES

diminution in infection has also played a role. Chlorosis—the green sickness very prevalent till the beginning of the century—has also disappeared because of diets more rich in iron, and perhaps also for other reasons connected with general hygiene. But no great advances could be made until a clearer appreciation was gained as to what constitutes a balanced diet. This was achieved largely in the present century by abandoning haphazard experiences in feeding for the experimental exploration of the problems of nutrition. Rickets with its mutilating deformities and diminished vitality was soon brought under control, and there is the prospect of overcoming pellagra, that dread affection in which masses of people in endemic areas are reduced to walking horrors—living skeletons held together by putrescent skins and propelled by deranged minds.

4. The science of dietetics

The food the body needs is not constant in quantity or quality. The body is never at rest, but also never placed under identical energy-consuming conditions. At rest, the heart still continues to beat and respiration still goes on; on the average a man resting in bed consumes 68 Calories per hour, 100 Calories when sitting at rest, 200 Calories when walking slowly, 240 Calories when engaged in such a task as carpentry, twice that amount when sawing wood, and 570 Calories per hour in running. (A Calorie is the unit of heat necessary to raise the temperature of one litre

of water by 1° C.; rather more than 100 Calories are necessary to convert a litre of water at 0° C. to steam.) But the rate of consumption of energy is not a constant; the body consumes more energy during growth, in cold weather, and under increased metabolic activity as is induced by Graves' disease and fever. In semi-starvation the bodily processes are slowed down and the energy consumption decreases. Estimates of 3,000 Calories or similar amounts as the minimum requirements of the body per day are therefore only approximate averages.

It is not just fuel but utilizable fuel that the body requires as food. Chemically six constituents in the food supplying energy are necessary : proteins, mainly derived from animal sources; fats, from both animals and plants; and carbohydrates, largely from plants; in addition water, mineral salts, and vitamins are essential.

Fats are the most economical fuel (9.3 Calories per gramme), proteins and carbohydrates being less than half as effective as sources of energy (4.1 Calories per gramme), but proteins are essential to replace the wear and tear of the body. 'Fat burns in the flame of carbohydrates; if there is no fire it smokes'—and the 'smoke' of fat consists of incompletely burnt-up fats (acetone bodies), which are poisonous to the body. It is these acetone bodies that produce the disturbances in diabetes which lead to diabetic coma, for in diabetes the patient cannot burn up his carbohydrates and thus provide the flame for burning his fats.

Proteins are uneconomical for the supply of energy, but serve to stimulate the whole process of energy consumption and supply ingredients essential to growth and life. Water accounts for about 60 per cent of the weight of the body, and its constant loss through the skin, lungs, and excretory organs has to be made good. Deficiencies in mineral salts and vitamins lead to specific disturbances.

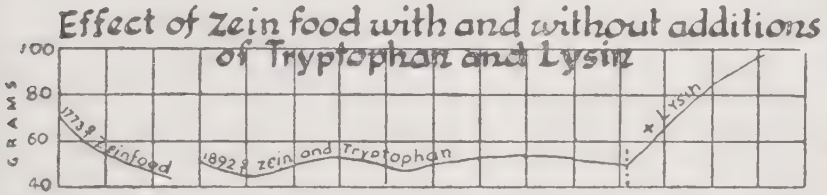


FIGURE 21. THE EFFECT OF VITAMINS ON LIFE AND GROWTH

There is nutritive decline on zein food, maintenance after addition of tryptophane, and growth after addition of both tryptophane and lysine. These are all amino-acids, the components of protein food. Each square represents 20 days of experimental observation. Though growth was inhibited in rat 1892 for a year and a half, the capacity to grow remained, full adult size being reached on feeding with lysine at the end of the experimental inhibition.

Some forty-one substances, apart from oxygen and water, are known to be essential components of food. Eighteen of these are amino-acids derived from proteins, eleven are inorganic elements, including calcium, phosphorus, and iron, ten are vitamins, the remaining two being glucose, derived chiefly from carbohydrates, and linoleic acid from fats.

No single food contains all the necessary factors, nor does any single protein contain all the necessary

amino-acids. Zein, the protein from maize cannot by itself maintain life; the addition of tryptophane to zein supports life, but in the young animal there is no growth unless lysine, another amino-acid, is added (Fig. 21). The remarkable capacity of the body to maintain its inherent qualities under adverse conditions is seen from the experimental observation that while the feeding of a rat on a defective diet will prevent its growth, this will yet proceed unimpaired if the lacking factors are added even after five hundred days (more than three-quarters of the average life of a rat). Minor degrees of ill-health develop on a diet ill-balanced in its protein; severe protein-starvation is illustrated by the horror of 'famine oedema', in which the emaciated body shows fantastic general or local swelling from water-logging of the tissues.

Amongst the mineral elements, sodium is necessary to maintain the normal neutrality of the blood; calcium is needed for the growth of bone, the formation of milk, and the maintenance of the contractibility of involuntary muscle; iron is required for the carrying of oxygen by the blood; and iodine for the proper functioning of the thyroid gland. A nutritional anaemia is a common disorder in pregnant women subsisting on a poor diet, more particularly as the expectant mother requires more iron than the non-pregnant woman. This anaemia, persisting during the period when the child is breast-fed, induces the same condition in the suckling. A lack of iodine—

generally in the drinking water—is responsible for goitre as an endemic disease.

The vitamins are accessory food factors; they do not serve as sources of energy, but their presence in small quantities is essential for health, growth, and even life. They are complex organic substances. The number of recognized vitamins is constantly increasing, the chemical structure of many is known, some have now been synthetized in the laboratory, and their physiological effects studied, but there is as yet little knowledge of their interrelation between the various vitamins and their integrative action in the body.

Clinical and experimental observations beginning at the end of the last century led to the recognition of the fact that deficiency of some factor in a diet otherwise balanced for the supply of energy leads to grave disorders. Beri-beri is a paralysis noted among peoples subsisting on diets of polished rice; a similar condition can be reproduced in birds by such a diet, and prevented by the addition of extractives of the husks of the polished rice. That minute quantities of some accessory food factors were essential to health and life was also learnt from the fact that animals on a balanced diet of proteins, carbohydrates, and fats (which fully satisfy their energy requirements) did not thrive; the addition of milk in quantities that could not materially affect the sum total of energy supply led to normal health. From these general observations there has developed the present-day

knowledge of vitamins.

Laboratory experiments reveal a great range of disordered states that can be produced by the absence or deficiency of particular vitamins. It must, however, be recognized that the artificial imbalance in diet produced in the laboratory is not necessarily a counterpart of dietetic deficiencies met with in life. A human diet is unlikely to be defective in just one essential constituent, and the clear-cut pictures obtained in the laboratory indicate rather than reflect human disorders. Even so, knowledge of the role of vitamins has led to the recognition that the absence or deficiency of vitamin D is responsible for rickets; that some fraction of vitamin B is essential for the prevention of pellagra; that vitamin A is necessary for the prevention of xerophthalmia, a cause of much blindness in the East and on the European continent during the first world war; and that this vitamin is essential to avoid changes in the tissues which facilitate such infections as pneumonia. The range of effects is indeed exceptionally wide; it is now known that vitamins A and both B_1 and B_2 have a marked influence on the nutrition and proper functioning of the nervous system; B_6 controls the nutrition of the skin; vitamin C is essential for the normal life of the cell, as it is part of the oxidation-reduction system on which cell life depends; and that other vitamins—probably no less than ten out of fifteen so far isolated—all have characteristic and essential functions.

To isolate vitamins from each other and from the

sum of energy-producing food is essential for laboratory methods, but man normally obtains his vitamins from his food and not as laboratory products. The problem of nutrition, and the whole question of health must therefore be viewed as a coherent whole. The laboratory can only indicate standards and remedies for isolated defects.

Dietetic balance therefore involves many factors not readily reduced to a standard recipe, as the great variety of national and racial diets show. On the basic issue of health and growth only now is empiricism being abandoned. History, tradition and ubiquitous poverty, rather than medicine, have so far guided dietetic wisdom and folly.

5. Diet and disease

Apart from undernutrition and defective nutrition, overfeeding and the intake of noxious substances present difficulties. Overfeeding shows itself in obesity and the mental and physical consequences which follow in its train. While the body will dispose without harmful effects of a limited excess, the inevitable ultimate result of overfeeding is the deposition of fat in the tissues, hampering their efficiency. Deposition of fat within the heart muscle reduces the working capacity of the body as a whole, limiting exercise and thus establishing a vicious circle of lowered bodily activity when a greater activity is necessary to burn up the surplus food.

A more obscure and probably more fundamental

issue is the ingestion of substances that have other effects besides supplying energy. While knowledge has accumulated on the significance of factors necessary for the maintenance of health, little is as yet known of the secondary effects of some food substances. Experimentally cholesterol induces arteriosclerosis (hardening of the arteries) in rabbits, and it is an important question whether excess of cholesterol —which is so richly present in some foods such as eggs—may not be a causal factor in that widespread and disabling condition. Hardening of the arteries is regarded as a normal feature coming on with advancing age, and it has been aptly said that a man is as old as his arteries. If our food can determine our healthy growth and existence it may also be that some constituents of it determine developments which are not inherent in our lives but superadded. An extreme example of what may be induced by an unsatisfactory food is lathyrism, a condition not unknown in Europe and seen with appalling frequency in areas ravaged by poverty, famine, and drought. The lathyrus pea on which the populations of such areas are driven to subsist contains a poison which produces paralysis. (In one year (1922) some 60,000 people were affected in Nepal, India). Inevitably the science of nutrition will have to concern itself with more than the avoidance of deficiency diseases, or with diets inducing slow poisoning, or with the maintenance of standards of health measured by past achievements. The recognition that food is not a passive entity, but a

stimulus operating on the body for good or for ill, takes nutrition to the stage when a more rational approach to the feeding of inviduals and nations will lead to the purposive building of health and not mere avoidance of disease.

6. By the sweat of thy brow

It is not only by the food he obtains or fails to obtain that man abuses his body; it is also abused in the struggle for food and other necessities for survival. The overcrowded, ill-ventilated slum does not supply the necessary conditions of cleanliness and fresh air essential for the proper functioning of the body, and this is reflected in the greater morbidity and mortality of slum dwellers. The result does not, of course, arise from isolated factors but from a series of associated conditions; poor living conditions generally imply poor nutrition and all the concomitant effects. The ill-ventilated mine destroys health as definitely as it destroys life in the occasional tragedy of a mine disaster. Industrial accidents are, only the highlights in a process that goes on continuously in all that man does to gain his sustenance. The more acute industrial diseases have been eliminated to a large extent. Such dread affections as 'phossy-jaw'—a spreading inflammation of the jaws of match workers employing phosphorus—and wrist-drop—a paralysis seen in lead workers—have been abolished by the substitution of less noxious raw material, but industrial occupations still take a

heavy toll in life and health. Anthracosis and various forms of chronic poisoning can be correlated with certain occupations or conditions under which the work is done. In printers between the ages of twenty and thirty-four years the mortality rate from all causes is 218 against the comparative standard rate of 100 in clergymen; the comparative mortality rate from tuberculosis of the lungs is 402 and from pneumonia 200. The sickness record of cotton operatives varies with the type of work: cardroom workers suffer three times as much from respiratory diseases as other spinning workers. In the final analysis the selective factor of certain occupations attracting certain types of physique has to be considered, but this only emphasizes how man and his work interact on each other. The hours of work have a marked effect on the incidence of accidents and morbidity, while the food and living conditions that man obtains by his work in turn affect his capacity for work and his ability to avoid and withstand abuse of the body.

As yet industrial hygiene deals only with the more blatant abuses of the body of man struggling for his bread. A purposive creation of optimum conditions for the work of man is only slowly emerging from the beginnings made in the elimination of specific noxious factors. The industrial age has produced architects of factories and engineers of machines, but it has still to produce architects and engineers of factory life.

In the abuse of the body, food and the means of ob-

taining it dominate over other factors. The high blood-pressure of the hectically living individual, and the 'athlete's heart' are examples of the body's reaction to stresses and strain induced by a mode of life at a pitch beyond that to which the body is adapted. A balance in diet, a balance in social environment, and a recognition of man's limitation within given conditions are all necessary considerations if the body is to be the tabernacle of the spirit of man and not its festering prison.

CHAPTER VI

Disease: The Assaulted Body

1. Protection against danger

The history of civilization is largely the record of man's struggle against deleterious factors in his environment. He must either insulate himself from such factors, adapt himself to them, or overcome them. To maintain and extend his supremacy man must therefore understand not only himself but the world in which he lives, for his body is not a passive unit in a passive environment.

Early man had to develop the rudiments of clothing and shelter in his struggle against the inclemencies of nature, and also means of defence against physical extinction by stronger animals. These imperative necessities, no less than inherent gregariousness, dictated the development of social life. In turn social life brought man's body in contact with new factors, some detrimental to his well-being. Overcrowding and the problems of sanitation can only arise in a settled community.

The cruder inclemencies of nature present no problem to day. There are no tigers and snakes in the

paved streets of cities; shelter, clothing, reservoirs of water and stored food counteract the more violent caprices of nature.

But man's environment consists of more than a medley of climatic conditions and fierce animal life. Behind his successful resistance to the more crude assaults of nature lies man's infinitely less successful resistance to subtler attacks, not on his body as a whole, but on its various mechanisms. Metaphorically speaking, he is only beginning to devise for his cells shelter and clothing other than those with which nature has supplied him.

The one-celled organism, when brought in contact with some substance outside itself, may remain indifferent to it. More frequently there is an interaction which results in either absorption of the substance into the cell, to be built into the cell-body or be broken up into innocuous ingredients, which are extruded; or alternatively the foreign substance overcomes the cell, making it so much dead organic matter to serve as food for other life. In such highly integrated multicellular animals as man comparatively few cells are exposed to haphazard environment, but the protection that the relatively constant internal environment of the human body gives to its constituent cells is not complete. The cell has still to face intrusions from without; and a disharmonious intrusion means death or disease.

Insulation against intrusion and consequent assault is highly developed in man, the insulation consisting

of skin and the mucous membranes. The skin is an effective barrier against substances which are lethal if they reach the interior of the body. A breach in the skin such as is made by the bite of a snake is necessary if the snake poison is to destroy man; or there has to be a wound, though perhaps no bigger than a prick, if infecting microbes are to set up a generalized infection. Likewise ingestion of noxious substances does not necessarily lead to disaster. Vomiting and diarrhoea induced by irritant poisons leads to the elimination of much of the poison, whilst organisms producing disease do not necessarily survive the action of the digestive juices secreted by the intestines.

The process of digestion is also part of the mechanism by which the body protects its cells from noxious agencies. While the uni-cellular organism is exposed to complex proteins in its environment, the cells of man have to deal not with the complex proteins taken as food, but with the simpler amino-acids into which the digestive tract has broken them down. Moreover, the process of digestion frequently serves to convert toxic substances into harmless derivatives, which are excreted.

When intrusion through skin and mucous surfaces does occur dire consequences may follow. This is exemplified by the reaction to complex proteins. Egg-albumen, which is an excellent food when taken by mouth and broken down into simpler amino-acids by the alimentary canal, may lead to death if injected

under the skin and so absorbed as complex proteins into the blood-stream—a result that can easily be achieved experimentally if an animal is first sensitized by a previous injection of the same substance (anaphylactic shock). The insulating mechanism of the skin and mucous surfaces of the multicellular animal safeguard its interior cells from agencies to which the unicellular animal has to react frequently and not always successfully. It reduces to smaller dimensions the huge outside world swarming with dangers to cell-life and to the organic whole made up of specialized cells.

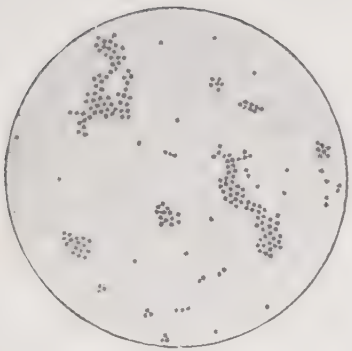
2. The microbe

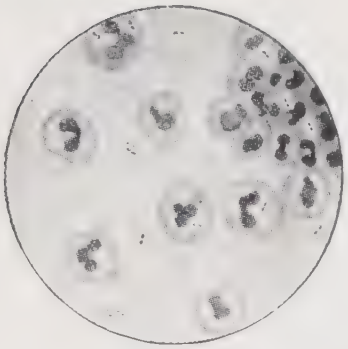
Among these dangers microbes have a special place. Only an infinitesimal part of microbial life is disadvantageous to human life. Much of microbial life is indifferent to human life in the sense that human tissues do not form a favourable environment for its existence, and therefore no tangible interaction between it and man can occur. Some of it is highly beneficial to man—directly, such as the organisms that are normal inhabitants of the alimentary canal and help in the digestive processes; and indirectly, such as the organisms that help life processes in general by their action on the soil and on dead organic matter (this liberates nitrogen and so keeps the cycle of vegetable and animal life in motion). The small group of microbes that interact

unfavourably with human life are important not by any scale of nature, but only in relation to man (Plate II).

Pathogenic (disease-producing) organisms are not rigid entities carrying destructive forces, which they liberate expressly for the destruction of human life. Like all other organisms they are living forms struggling for survival, and their effect on man is incidental to their own life and not due to planned malice. From man's point of view they are foreign proteins against which he has a considerable power of insulation, and defence when insulation fails; but they are also proteins with some special qualities. In the first place the protein is alive and capable of multiplication, thus introducing a quantitative factor in a qualitative problem; and secondly the protein is capable of liberating substances deleterious to the body (toxins).

Disease is never the result of unaided efforts of the pathogenic microbe. Indeed, there is no hard and fast line separating the pathogenic from the non-pathogenic organisms; microbes pathogenic for animals are not ordinarily pathogenic for plants, and only a few of those that are pathogenic to mammals are so to cold-blooded animals. The infections that kill man have no effect on wild carnivorous animals (which are prone to few bacterial diseases), and many organisms that are highly destructive of animal life do not harm man. This restricted action of bacteria is parallel to the restrictions seen in inanimate poisons: strychnine,





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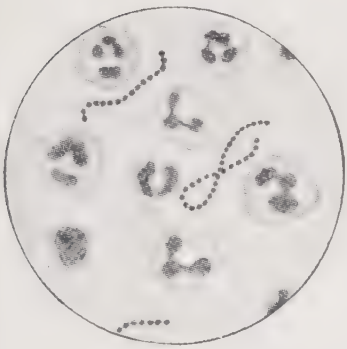

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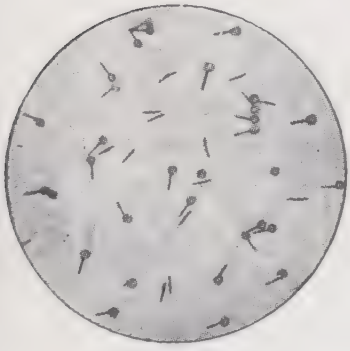

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PLATE II. SOME COMMON MICROBES

1. Staphylococci. 2. Pneumococci, some free and some being ingested and destroyed by white blood corpuscles. 3. Streptococci and white blood corpuscles. 4. Typhoid bacilli. 5. Diphtheria bacilli. 6. Anthrax bacilli. 7. Tetanus bacilli. 8. Spirochaete in liver tissue in congenita syphilis.

which is so poisonous to vertebrate animals, has little effect on unicellular organisms, just as quinine kills the malarial parasite with little effect on the tissues of the infected host.

Disease is thus not inherent in the microbe: it is an aspect of the interaction of the microbe and its host. Even so, the conditions under which interaction can occur are strictly limited by biological considerations affecting both the parties, and by the secondary effects of the interaction once it has occurred.

The simplest pathogenic effect of a microbe on man is that seen when the microbe does not affect the living body directly, but produces disturbances by the toxins it *elaborates* when it grows on dead tissue with which the body comes in contact. Botulism is a form of food poisoning caused by the ingestion of food infected with *Bacillus botulinus*. The infected food carries to man the toxins of the bacillus, and may kill by acute poisoning. Here there is no direct interaction between the microbe and man, for the *Bacillus botulinus* cannot exist in living tissue. Rather similar are the disorders produced by the tetanus bacillus and the diphtheria bacillus. The toxin of the tetanus bacillus is highly poisonous—about 150 times more poisonous than strychnine and about twenty times more than the venom of the cobra, the most poisonous of snakes. The tetanus bacillus is not usually capable of maintaining itself and multiplying in healthy tissue, and its killing effect is due to the toxins it produces in the wound into which it has

been carried. Diphtheria too acts largely by liberating toxins which are absorbed into the system.

The biological characteristics of microbes are, however, exceedingly fluid. Though the tetanus bacillus cannot thrive on healthy tissue, a slight change in the tissues enables it to do so. Such changes may be induced by damage of the tissues, by the presence of foreign bodies or of pus-forming organisms. Moreover, the capacity of a microbe to induce an effect (virulence) is very easily modified both in nature and in the laboratory. Drying or exposing to abnormal temperatures may modify or destroy virulence, and by various methods of culturing organisms their virulence may be either increased or diminished. This increase or diminution is a strictly relative process. If increase is obtained through rapid culturing of a particular organism by successive inoculations into a series of animals of the same species (i.e. the microbe is cultured in successive 'living test-tubes'), that increase is not usually a general characteristic but is limited to that particular species of animal. In fact the virulence for other species may be diminished, as when successive inoculations of the virus of rabies into rabbits will make it more virulent to rabbits but less virulent to man, or as when certain streptococci may be made more virulent to mice and simultaneously they become less virulent to rabbits.

There are thus conditions when the non-pathogenic microbe may become virulent to man, and a mildly pathogenic organism develop high virulence. This is

exemplified daily by the occurrence of human disease arising from organisms that normally live on or in the body without causing disturbances. But it is not only an enhanced virulence on the part of the microbe that is responsible for such events; the reaction of the host is also of prime importance. When a normally nonpathogenic organism produces disease, a disturbance in the precarious balance between microbe and man has occurred. The protective forces in man are no more a fixed entity than the biological characters of the microbe are.

3. Bacterial infection

Man's protective forces are his insulating mechanisms—his intact skin and mucous surfaces—and the complicated processes of immunity and defence that are able to repel and destroy invading organisms. These are all factors that are highly variable and limited. The insulating mechanism of an intact skin is effective against the microbe of cholera, and a breach in it will not render him a victim to cholera, but the mucous membrane of the alimentary canal is a poor defence against invasion by cholera; a breach in the skin destroys the barrier against streptococci and may lead to death, but the mucous membrane of the alimentary canal is constantly destroying virulent streptococci. The individual's immunity is a highly changeable feature. There is evidence that immunity to certain assaults is an inherited condition, as is suggested by the resistance of some children to some

infective conditions. Individual variations in immunity are, however, largely determined by extraneous conditions. Hunger and thirst reduce immunity, as can be seen from the fact that pigeons, which are normally immune to anthrax, can be killed by anthrax bacilli if the inoculation is done after the birds have been kept on a low diet; extremes of heat and cold have the same effect—frogs, immune to anthrax at normal room temperature, quickly succumb after inoculation at a higher temperature. The greater prevalence of pneumonia in winter and of infections of all sorts in the debilitated illustrate the same tendency. Experimentally the same effect is seen when the white rat, which is highly insusceptible to anthrax, succumbs to inoculation if it is fatigued and exhausted by work in a treadmill. Children possess less immunity to infection than adults; this is apparent in the prevalence of certain infections as almost exclusively children's ailments, and in the fact that the mortality rate is higher in affected children than in adults: in one series of 70,000 cases the mortality rate of scarlet fever in children under five years was 18.2 per cent against 2.8 per cent among adults aged twenty to twenty-five years.

To produce disease both general and local conditions must favour the invading microbe. For the tetanus bacillus to establish itself the local factor of damaged tissue is essential. Diphtheria is much more serious if other organisms damaging the local tissues are also present at the site of infection, though these organ-

isms by themselves would be relatively innocuous. Tuberculosis of the lungs is more likely to develop in an individual working in an atmosphere laden with irritating dust. Moreover, some bacteria can thrive only in strictly limited conditions; the gonococcus can establish itself only under the local conditions present in the genital tract and the mucous surfaces of the eyelids and the nose; the organism of syphilis, though capable of invading healthy mucous membrane, cannot penetrate intact skin.

Infection is thus a highly organized process which can take place only when a specific microbe of sufficient virulence can establish itself in the presence of suitable local conditions and the failure of immunity reactions to prevent the organism from gaining a foothold. Some organisms, like the bacilli of botulism, diphtheria, and tetanus, are either completely incapable of living in the body or do so under conditions not very favourable to their propagation. Such organisms, as already indicated, produce disease by the toxins they secrete. Most pathogenic organisms do, however, find in the human body suitable conditions for their existence once they gain access through a breach in the skin or mucous surface. Certain organs are particularly suitable for certain microbes: anthrax grows luxuriantly in the spleen, and glanders bacilli, when injected into the peritoneum of a male guinea-pig, localize with such regularity in the testicles that the experiment has a diagnostic value. Generally the blood-stream is a poor culture

medium for the invading organism, and localization of the infection at particular organs is largely determined by local conditions: thus in rabbits staphylococci do not normally settle on the valves of the heart, but will do so if in addition to a blood-stream infection the animal has been subjected to slight damage of the valves. Under normal conditions the localization of infective disease into special organs does, however, indicate a biological feature of the invading organism. The tendency of the staphylococcus to form multiple abscesses is such a feature, just as the widespread dissemination of the streptococcus without a tendency to abscess formation is an opposite characteristic. This localization determines characteristic clinical pictures or 'diseases', but as the tendency to localization is readily influenced by a variety of conditions clinical pictures are apt to show considerable departures from an idealized conception ('atypical' cases).

The invasion of the blood-stream by microbes opens the cell-system of the body to the presence of foreign proteins that are constantly multiplying and to the toxins produced by these living foreign proteins. Sometimes, as in diphtheria and tetanus, the toxins are freely poured out and constitute the essential feature of the disease, the organism itself being relatively unimportant. In other instances, as in tuberculosis, the toxin is locked up within the microbe and its effect becomes apparent only when the microbe is disintegrated by the defence mechanism of the body

—the protein foreign body that the organism constitutes is here an important feature in producing the disturbances of disease.

4. Resistance

When an invading organism overwhelms the defences of the body and its toxins are highly poisonous, death rather than disease is likely to follow. Disease in such cases is a manifestation of resistance, and the localization of disease in a particular organ is the expression of a specific local reaction in the general resistance. If pneumococci are introduced into the lungs of such a highly susceptible animal as the rabbit the animal dies quickly from a generalized infection, the pneumococci having passed into the blood-stream without exciting much reaction in the lungs. If the animals are first rendered more resistant to pneumococci by special methods of immunization they develop not a fatal spread of the pneumococcus into the blood-stream, but pneumonia, which is thus to be regarded as a violent and successful reaction by the lungs. Other organisms besides the pneumococcus are resisted by the reaction of the lungs, so that pneumonia is not a disease produced by the pneumococcus, but a manifestation of a defensive mechanism by the lungs against the pneumococcus and other microbes (such as Friedländer's bacillus). Similarly a severe local reaction around a prick in the finger represents a local defence mechanism against invasion; the mechanism may fail and the

patient die, but the absence of a local reaction is of the gravest significance in a patient who becomes ill after such an accident, for it implies a failure of local defence in the first instance and the passage of the infecting organism into the general circulation.

The complicated mechanism of resistance and immunity is essentially an elaboration of the defensive mechanism that all living cells have against disharmonious intrusions. In its defence the body acts as an integrated whole, though special organs supply special defensive agencies. The white blood corpuscles are capable of digesting invading microbes and the body fluids produce substances that help the white cells both directly and in inducing an environment unfavourable for the survival of the microbe. This results from the fact that specific stimuli, such as the protein of the microbe body and the toxin the microbe produces, induce changes within the cells and body-fluids that are inimical to the continued existence of the exciting stimuli (antigen-antibodies formation). The defence mechanism thus induced is an illustration of the universal biological law that everything is self-limiting, that there is no unchecked activity in Nature, for each process produces factors which militate against its uncontrolled increase.

The self-limiting character of infectious disease is clearly seen in epidemics. With an increase of virulence in certain pathogenic microbes (from inherent factors or a change in environmental conditions or a lowered immunity in the human population) an epi-

demic breaks out. In these circumstances virulence is likely to increase still further, because of the prevailing conditions, which correspond to the laboratory experiment of exaltation of virulence by rapid passage through animals of the same species. The increased virulence may convert an epidemic into a still more extensive pandemic, but inevitably a decline must follow, for three reasons : (1) a certain number of affected individuals succumb; (2) the survivors develop immunity to further attacks; and (3) the unaffected population must originally have been insusceptible and are thus not liable to infection.

Once the body has suffered invasion of proteins or bacteria it carries for ever indelible memories of the assault. Both a quickened sensitiveness and a greater defence against further assaults always follow a repelled invasion, but frequently there are also the scars and wreckage of battle.

The quickened sensitiveness and greater capacity for defence are two aspects of what is fundamentally one process. Anaphylactic shock, allergy, and immunity, though strikingly dissimilar as isolated phenomena, are all different expressions of the capacity of resistance. Underlying these reactions is the production of antibodies to neutralize the invading protein or microbe. The production of antibodies implies the body's recognition for their need, and in terms of cell behaviour implies a greater sensitiveness to the existence of those stimuli that call forth antibody formation. This is the basis of allergy, in which the

patient is more sensitive to certain proteins or bacteria. The sensitivity is, however, not one-sided; it goes hand in hand with a greater capacity to overcome that deleterious factor to which the body is sensitive; and it is this which constitutes immunity. Allergy is thus a phase in immunity.When the achievement of immunity (by the production of antibodies) lags behind the promise of allergy, the patient has become more sensitive to invasion without a corresponding increase in his capacity to repel it; when the promise of allergy matures in a rich immunity, the greater sensitiveness of the body to the exciting stimulus is more than balanced by the greater capacity to overcome it. But as allergy and immunity are not independent processes, all sorts of intermediate phases between dominance of either the allergic or the immunity phase occur, and different clinical pictures are produced in the body as these labile forces wax and wane. The great range of manifestations of tuberculosis are an excellent illustration of this process. Most people have been infected with tuberculosis by the time they reach adult life. As a result they are more sensitive to the tubercle bacillus, and this can be demonstrated by their reaction to the tuberculin test; an uninfected individual gives no response, an infected individual shows his sensitivity by a localized skin reaction around the injected tuberculin. Infected adults are thus allergic to tuberculosis, but they are not victims to the disease because in most cases the consequent immunity is greater than

the allergic sensitivity that induces it—the body, though more sensitive to the tubercle bacillus, is also more effective in disposing of it. Where the immunity does not clearly overshadow the allergy, mild 'atypical' manifestations of tuberculosis develop, and a whole range of previously obscure disease-processes are now recognized as the expression of an uneasy balance between tuberculous allergy and immunity. In the course of such diseases periods of quiescence or activity occur corresponding to the dominance of immunity or allergy at those particular periods. Where allergy clearly overshadows immunity the development of frank tuberculosis is inevitable: the tissues have been lured to greater sensitivity by an unfulfilled promise of greater immunity. It is not the greater sensitivity but the unfulfilled promise that determines disaster.

Microbial invasion is thus repelled in a number of ways. The toxin of microbes stimulates the production of antitoxins in the body; and the microbe itself stimulates the development of antibodies that tend to make its own continued existence impossible. Action and reaction are rapid in the acute infections, whilst chronic infectious disease is a slow-moving biological play with heavy-footed actors.

The memory that the body carries of previous assaults sometimes finds expression in permanent memorials in the shape of damaged organs: this is inevitable in chronic infections such as tuberculosis and syphilis, where the tissues are damaged in the course

of the slow drama of the overwhelming of the invading organism. Much of the damage is repaired by the normal reparative processes of the cells of the body, but highly organized tissues cannot be replaced fully by repair. Secondary effects frequently arise, as when the repair of damage in arteries caused by the organism of syphilis leaves not a normally functioning vessel but one with the walls showing many weakened areas. The normal pressure of the blood within the weakened artery may lead to localized bulgings (aneurysms) and ultimately actual rupture in such a bulge. Ruptured aneurysm of an artery in the brain is one of the less common causes of stroke, while a ruptured aneurysm of a big artery like the aorta leads to instantaneous death. The full cycle of assault by microbes sometimes ends in unexpected anatomical and temporal remoteness.

The body may also carry scars of battle from an intensive invasion which has been repelled. Rheumatic fever in childhood may not appear to be a grave affection, but a biological feature of the organism of the disease is a localizing tendency in the muscle and valves of the heart. Severe damage may be done in the acute phase of the invasion, but frequently a relatively mild process is initiated which does not give any apparent trouble for many years. The accumulation of mechanical difficulties of the damaged heart and a whole series of secondary effects may in the end cripple the patient. Much chronic disease is a slowly maturing legacy from a forgotten source, but

though the mind of man can forget, the body remembers everlastingly.

5. Infectious disease in the scheme of things

Bacteria are neither enemies nor friends of man. There is evidence that the completely sterile body could not function, and man's interaction with the world of the infinitely small is only a part of his interaction with the outer world as a whole. In that scheme infectious disease is but an accident: conditions arise under which an harmonious relationship becomes disturbed because of changes in the outer world and in man himself. When the balance of forces is against man death ensues; when the balance is level or nearly so a struggle for readjustment occurs and is made manifest by the disturbance of disease. In the final analysis infectious disease is the struggle between an integrated cell system against more lowly organized cell units. It is one further manifestation of the endless adjustment of living things to each other and to the outer world.

To unpurposive animal life infectious disease is an inevitable aspect of existence and operates as a very pruning-hook of nature. To man it is one of a series of imbalances that he has consciously rectified and ever continues to rectify in his favour.

CHAPTER VII

Treatment: Individual Measures

1. Empiricism

Man is a panicky animal as well as a rational being, and his mind is so constituted that in a crisis the call for action is more tumultuous and urgent than the need of understanding the crisis. It is thus that treatment, being rooted in a primitive need, is older than any systematized studies of disease, while man's capacity to observe and to reason accounts for the two-fold strand of empiricism and logic that has run and still runs throughout all systems of therapeutics.

Empiricism with its reliance on proved observations is essentially a hit or miss method. The hits it has scored have given medicine some of its most valuable means of treatment : rest in disease; drugs like opium, quinine, mercury, and digitalis in some affections; and a whole body of practices that profoundly influences all treatment. As against the hits, empiricism is responsible for an endless amount of sterile effort, and much diversion from its own straight and narrow road—for empirical practices, finding their sanction

in tradition, have often flourished by virtue of a fortuitously built-up but inherently unjustifiable traditional approval.

Formal logic applied to treatment has been infinitely more barren of results. It has given the sanction of reason to the most fantastic conceptions, and could not do otherwise as long as the premises on which the logical superstructure was built were themselves irrational. Without the straw of rational premises, logic could make only chimerical bricks. It was thus that logic gave sanction to the casting out of the devil —by the beating of tom-toms or by priestly exorcism or by the modern prayer meeting; these are all logical procedures if it is accepted that disease is due to posession by an evil spirit. Logic was responsible for a series of nightmare systems of therapeutics that different ages based on the prevailing conception of the universe. It was thus that blood-letting on a heroic scale found a logical justification in the humoral theory of disease prevalent among the Greeks. But the Greek excursion into heroism paled into insignificance when, after more than twenty centuries, a new logical justification for bloodletting was advanced on the basis of a philosophy that saw disease as the expression of local irritation and found treatment in depressing measures. In one year (1833) France imported forty-one and a half million leeches and it is difficult to estimate the damage that was done before the torrents of blood were stemmed by the slowly operative forces of empiric validity.

Logic is no more self-sufficient than is anything else in the universe. It is but the key to the labyrinth of existence, and it can lock as well as unlock. The logic of insanity is as consistent as it is terrible; and the triumphs of the logic that builds on valid premises has its obverse in the devastations achieved by the logic that built therapeutic systems on unquestioned assumptions. The essence of the scientific method lies not in its use of logic, but in linking it into a unity with the observed phenomena of nature. Philosophically this involves the acceptance of a material universe and a recognition that our sense-perceptions of things give a working knowledge of that material universe. To go beyond that and to admit idealist considerations is to hand over man's achievements to the most disruptive forces in existence: imagination and reason unchecked by reality.

In the scientific method—and modern medicine is only one of the many applications of it—empiricism has thus an unquestioned place. An isolated observation is, however, not empiricism; only accumulated observations indicating the same trend, checked again and again and reducible to a generalization, constitute an empiric truth. Reason can systematize empiric truths, disclose unsuspected links, and build the whole into a more-embracing generalization, which in turn leads to the easier exploration of empiric findings and to rational deductions which furnish a still more embracing generalization. Yet on the fringe of such synthesizing processes there are always ill-fitting

observations, the validity of which cannot be doubted. Often the accumulation of such observations leads to the drastic revision of conceptions that appeared rooted for all time. In physics Einstein's work could mature only with the accumulation of ill-fitting facts collected around the Newtonian conception of space; in medicine the conception that microbes are the cause of all disease could not be maintained in face of the discovery of the ill-fitting facts that the study of heredity, the ductless glands, and nutrition revealed.

Empiricism in treatment has always groaned under superfluous accretions. The laxatives and enemata that the ancient Egyptians used were administered together with sacred ceremonies, incantations, and magic rituals, but in all such procedures man's mind could not always destroy that which was of permanent value in his collective experience. The sum total of what has been salvaged of that collective experience extending over millenia—shorn now of its smothering accretions—has become incorporated into modern medicine. Much of it has found a place in systematized rational knowledge; some of it is still beyond the reach of any logical explanation and has its place by virtue of well-attested empiric truth.

Though that which has been extracted from the empiricism and the ratiocination of the ages constitutes but a small fraction of modern therapeutics, it is yet of the greatest value. The use of suggestion in treatment is the direct offspring of the magic rituals of the past, and is of unquestioned value in a strictly

limited sphere of minor mental derangements. For the relief of symptoms, as opposed to the eradication of disease, modern medicine is heavily indebted to the past. In the treatment of pain the use of opium and its derivatives could not be established by any reasoning or by laboratory experiments. The mechanism of pain is still too obscure to allow any comprehensive approach towards its control, and the great variety of pain-relieving drugs now available all represent empiric efforts. Aspirin and its allied coal-tar derivatives were elaborated in the first place not for the relief of pain, but for other purposes, and their analgesic (pain-relieving) properties were an incidental finding. Many modern purgatives have a similar history. Anaesthetics came from chemical experiments by a circuitous route, for their properties, like those of cocaine and its derivatives, could not be deduced from any knowledge of their composition. Digitalis is still the most potent drug for some forms of heart disease, and its more modern substitutes represent direct applications of knowledge gained empirically. Long before the causal organisms of syphilis and malaria were known—indeed long before the microbial origin of these or any other diseases was suspected—mercury and quinine were successfully used without any knowledge of their bactericidal effect. Recognition of the importance of balance in food and some remarkably successful diets came long before the rational approach of modern medicine. The accumulated wisdom of the ages has

a message that modern medicine gladly accepts, refusing only the stammer, the splutter, and the shrillness in which it is couched.

Towards the middle of the last century the shrillness had all but distorted the words. There was as yet no coherent conception of the causation of disease; there were only vague and contradictory theories. Pharmacology (the experimental and clinical study of the action of drugs) was still in its infancy, and organic chemistry had not yet made any contribution towards the isolation and synthesis of pharmacological substances. There was little to draw upon except the flagrant polypharmacy that began with Galen and persisted throughout the centuries. The endless dosing with the weirdest of mixtures, such as *theriaca,* with its seventy-eight constituents (concocted for a Roman Emperor and still used in the nineteenth century), or with various mixtures of excrements of animals, had led in the eighteenth century to the useful revolt of the homoeopathists, who, however, floundered in similar bogs of absurdity. The fact that the homoeopathic bogs were shallower did not materially affect the position, for the arid winds of homoeopathy killed the flowers as well as the weeds. The therapeutic nihilism that had developed by the middle of the last century was, however, only the prelude to the luxuriant growth of modern therapeutics. Through the narrow-meshed sieve of therapeutic nihilism there was passed on only that which the experience of centuries had sanctioned: a few metals, a few plants,

much more in the way of common sense, and vaccination against smallpox—that tremendous portent of coming events that cast their shadow before. Empiricism had been purged of its dross.

2. The therapeutics of bacteriology

The jungle had been cleared, but it became a blossoming plain only after the tidal wave of bacteriology had broken over it. The laying bare of the microbial world as a cause of disease led to the search of means to control that deleterious life. To-day medicine draws on a complicated range of agencies that strengthen man's defences and weaken the microbe. The attack on the microbe has proceeded on two main lines: neutralization of its toxins and the extinction of the organism itself.

Neutralization of the toxin gave brilliant results from the very beginning. It was thus that anthrax, tetanus, and diphtheria came rapidly under control. The mechanism exploited in this approach rests upon the facts that the toxin induces the body to produce antitoxins and that these antitoxins persist in the blood-stream after recovery from the acute illness. The serum (i.e. the blood less its red and white blood corpuscles) of a patient previously affected thus has curative properties. Antitoxic sera are conveniently prepared by carefully controlled infections in animals. Thus diphtheria antitoxin is the serum of horses kept under hygienic conditions and infected with strictly controlled doses of the diphtheria bacillus, while

anthrax antitoxin is prepared from sheep. Animals that are susceptible to the particular organism for which an antitoxic serum is sought have to be employed, and sometimes only human blood-serum (immune serum) is available, as in measles and infantile paralysis, for these affections cannot be induced in animals.

The hope of producing specific antitoxic sera for all microbial disease was not fulfilled. In some cases suitably susceptible animals are not available, but more important is the fact that antitoxic sera are satisfactory only for those infections in which the toxin is more significant than the microbe. This narrows the range of utility of antitoxic sera to those affections, such as diphtheria, which are essentially a toxaemia (toxins circulating in the blood-stream) rather than a bacteraemia (bacteria in the blood). Antitoxic sera are not indeed without value in a bacteraemia, but they do not give the striking results seen in diphtheria and similar conditions.

Attempts to exterminate pathogenic bacteria that have gained a foothold in the body have proceeded along two distinct lines. Vaccination against smallpox was the empirical procedure that indicated the possibility of building up an active immunity. This consists of inoculation of the patient with attenuated (weakened) microbes or graduated small doses of their toxins to induce the formation of antitoxins against toxins and of antibodies against the microbes. The patient is in fact given a controlled and mild form

of the affection in question; the dangers and general disturbances are avoided and full use is made of the defensive mechanism called into being by what may be termed a sham attack. How successful this approach proved in rabies is common knowledge, but the use of vaccines is limited, for in acute disease no sham attacks are necessary. On the whole vaccines have proved of great value in preparing defence against infection or its development, and of little value in the actual treatment of the established disease.

For the extermination of bacteria during an acute infection, no adaptation of the normal antibacterial and antitoxic mechanisms of the body seems helpful. It is due to Paul Ehrlich, immersed in alchemist dreams and uneasy in the world of men, that another road was opened. The culmination in our days of the work he began over fifty years ago promises to relegate acute infectious diseases to the forgotten nightmares of history.

Ehrlich dedicated himself to evolving *therapia magna sterilisans*, the discovery of a 'magic bullet' that would free the blood and tissues from pathogenic microbes without harming the tissues of man. The facts that bacteria stain with dyes, and that some of these dyes are capable of killing bacteria (bactericidal) in a test-tube, led him to the exploration of dyes as agents that would combine with the microbe and destroy it. In test-tube experiments dyes that kill microbes could be found readily enough, but such dyes invariably had serious effects on experimental

animals. Even when dyes with a relatively high bactericidal effect and a low toxicity to animals or man were produced, it was found that in experimental infections in animals the effect of the dye was not at all what was expected from its isolated effect on bacteria or on the animal, i.e. the behaviour of the dye within the body of the infected animal was different from the behaviour of the component elements in isolation. The microbe in the blood or body of an animal or man is in fact a different entity from the microbe under other conditions. In patient exploration of various substances effective on different organisms. Ehrlich finally established trypan red as a substance satisfying the conditions he sought to obtain: it was lethal to the organism of trypanosomiasis and almost non-toxic to the infected animal. Three years later (in 1910) he brought forward an organic arsenic compound (salvarsan or 606) as lethal to the organism of syphilis, but well tolerated by man. The conquest of microbial life had begun.

The organisms of both trypanosomiasis and syphilis belong to a group of microbes that have special structural and cultural characteristics. Such successes as were obtained in subsequent investigations with chemical agents (chemotherapeutics) were confined to the eradication of similar or allied organisms, so that the view gradually grew up that chemotherapy as visualized by Ehrlich had no promise in the more common killing infections due to more lowly organisms. Septicaemia from staphylococcal or streptococcal in-

infections—puerperal sepsis or childbed fever is one of them—continued to exact its toll year by year. As far as these and similar acute infections were concerned bacteriology tended to become, not quite an academic exercise, but almost little more than a convenient guide to diagnosis and prognosis. All this was dramatically changed when, twenty-five years after the introduction of salvarsan and twenty years after Ehrlich's death, an accidental observation showed that a certain red di-azo dye was curative to animals infected with that most killing of microbes, the *Streptococcus haemolyticus*. What Ehrlich had foreseen but had failed to achieve had come about unexpectedly. A direct attack on all deleterious microbial life had become feasible. A vague hope had become a vision not of the possible or probable but of an inevitable achievement.

The original di-azo dye of fifteen years ago has now been replaced by a number of colourless derivatives (sulphanilamide and allied compounds), and a whole series of infections are now under control. Pneumonia no longer exacts the terrible levy on life that it did a few years ago; gonorrhoea and gonococcal infections of the eyes of new-born babies are easily cured; puerperal sepsis is no longer the haunting horror it was; and streptococcal infection, which previously was frequently fatal, has been robbed of its terror. No less significant is the drastic change in minor ailments. Sore throats in childhood are often complicated by middle-ear inflammation with slowly pro-

gressive secondary changes, and much deafness is a direct consequence of throat and ear infections early in life; all these and many more minor ailments are now readily controlled. The mastery over the microbes of common ailments is not merely a marked advance in life-saving measures; it is a manifesto to the future, a promise of life secure from sudden assault and purged of insidious marauders lurking in the inaccessible caverns of the body.

The mode of action of sulphanilamide and its derivatives is as indirect as its discovery was indirect. The sulphonamides do not kill the microbe by direct assault; they destroy *p*-aminobenzoic acid, a necessary ingredient in the food of microbes. When an infected animal is given an excess of this ingredient together with sulphanilamide the infection runs its inevitable and relentless course.

If the purely bacteriological approach to the conquest of infections by vaccines and sera produced limited, though by no means insignificant, results, and chemotherapy, as exemplified by salvarsan and the sulphonamides, has enlarged immensely the possibilities of treatment, there is evidence that the struggle against microbial life is now entering a third phase. The discovery of penicillin by Alexander Fleming has opened a new source of potent therapeutic agents, this time derived, not from the microbes themselves, nor from the chemical laboratory, but from the plant world. Penicillin has proved to have a wider range of action than the sulphonamides and

to possess an almost unique property in being free from any side effects, so that there is no fear of excessive doses. As it is highly effective in local use (in contrast to the sulphonamides) its range of efficacy and ease of handling is therefore exceptionally wide. To a large extent penicillin has already replaced the sulphonamides in treatment. In contrast to the sulphonamides it acts directly on bacteria.

Penicillin is ineffective against the bacillus of tuberculosis and allied organisms. Streptomycin — an allied mould extract — promises to supplement the action of penicillin as it is effective against the bacillus of tuberculosis. The clinical applications of streptomycin have still to be elaborated fully.

3. Endocrine therapy

The earliest success of ductless gland therapy—the treatment of myxoedema and of cretinism by thyroid gland—came at the height of the mental intoxication induced by the brilliant advances in bacteriology in the last quarter of the previous century. The development of ductless gland therapy suffered in consequence of the prevalent preoccupation with bacteriology, but the early trickle has expanded into a swirling flood. Endocrinology has given to modern therapeutics such substances as pituitrin, which has saved many women in labour; adrenalin, without which the treatment of asthma and other allergic conditions would be infinitely less satisfactory; cortin, a life-saving measure in Addison's disease; heparin,

for the prevention and treatment of clotting in blood-vessels; oestrin, which has overcome the pathos of the menopause; and various hormones for less clearly defined conditions. The treatment of diabetes has been revolutionized by the isolation of insulin, and diabetics can to-day lead normal lives, instead of being, as they formerly were, haunted shadows of themselves and a ready prey to all assaults.

Apart from the recognition of the necessity for a minimum of iodine in drinking water if thyroid gland disturbances are to be avoided, there is as yet little understanding of the factors needed for the normal functioning of the various glands and for their normal integration. The rich promise of a capacity to mould physique and personality lies in the further unravelling of these fundamental issues.

4. Nutritional therapy

The development of the science of nutrition has placed in man's hands, so far, not a recipe of food for gods, but the means of preventing the degradation of man to the grotesque. Rickets, with its hideous and dwarfing deformities, has been banished by the recognition and isolation of vitamin D; pellegra, a vitamin B_2 deficiency, need no longer haunt the sight and minds of its observers; xerophthalmia, scurvy, and a host of other conditions—some generalized, as certain nervous conditions, and others localized, as some corneal lesions—all respond to appropriate vitamin therapy.

Vitamin A, vitamin E, and vitamin K all illustrate the future potentialities of vitamin therapy, not in avoiding or rectifying structural anomalies, but in maintaining normal health and function. Some forms of night-blindness respond to vitamin A therapy; habitual abortion (repeated miscarriages) is occasionally due to vitamin E deficiency, while vitamin K appears to be an essential factor in eliminating some varieties of abnormal bleeding.

Apart from vitamin therapy, the science of nutrition has given to therapeutics experimental sanction for the use of iodine and of iron, but over and above all a clear recognition of the fact that not only the soul of man, but his body too, does not live by bread alone.

5. Possibilities in hereditary affections

Modern therapeutics has even broken through into the realm of hereditary diseases. Apart from malformations, for which surgical procedures are available, hereditary affections are becoming amenable to treatment as more becomes known of the underlying basis of these disturbances. As yet the nature of most hereditary diseases is unknown, though much has been learnt of their mode of inheritance. One group of rare recessive conditions has been established as disturbances in the fat metabolism of the body (the lipoidoses, such as Tay-Sachs disease, Christian-Schüller disease, and Niemann-Pick disease), and in one particular affection (Niemann-Pick disease), which was

previously invariably fatal, control of the fat intake in the diet is giving excellent results. Malignant jaundice of new-born babies (which is possibly another recessive condition) previously ended fatally, or reduced the survivor to imbecility and paralysis. Empirically it has been found that a blood-transfusion from the mother leads to cure. In acholuric jaundice, yet another recessive condition, the empirically established procedure of removal of the spleen likewise leads to cure. The suggestion that emerges from experience gained so far is that in some hereditary affections the condition that is inherited is primarily not the clinical picture presented by the affection, but some abnormal metabolic activity amenable to correction. A stumbling-block in the development of a satisfactory therapeutic approach is the general attitude, which still regards hereditary diseases as rigid unalterable entities instead of progressively unfolding processes, burnt out ruins instead of a smouldering flame, amenable alike to fanning or extinction.

6. Experimental physiology

Experimental physiology has supplied therapeutics with a series of valuable agents. From a study of the normal mechanism of the circulatory, alimentary, and other organs of the body, there has evolved the study of agents that modify normal action. It is thus that stimulants of the heart, of intestinal movement, kidney secretion, and other activities have been established, and some of these laboratory findings have found

application in clinical medicine. Mercurial diuretics depleting the body of excessive fluid, which is so distressing a feature in heart failure, have proved a life saving measure; though not curative, they have greatly simplified the treatment of this form of heart disease adding comfort as well as years to the lives of patients. Other drugs such as atropine, physostigmine, acetyl-choline, histamine, prostigmine have been evolved by this laborious method—a method stricty limited by the fact that it is still largely impossible to correlate chemical composition with physiological effect. Once it is established empirically that a substance with a certain chemical structure produces a characteristic physiological reaction, it is possible to attempt to combine chemical groups in order to obtain a desired result. This is the basis of much experimental work in pharmacology: chemical substances are devised for certain purposes, but generally the character of the new compound reveals unexpected properties. So far only minor successes have been achieved by this approach, and there is more scientific empiricism than scientific reasoning in these successes. As yet chemistry has been more successful in eliminating undesirable toxic effects from empirically established compounds than in consciously evolving chemical disciplinarians of the body in health and shock troops in disease.

7. Scientific empiricism

Stumbling after truth, with frequent failure to recognize it when it is met and hesitant avoidance of the pitfalls of half-truths, is the painful gait that characterizes the empiric method. Yet empiricism must remain a major line of approach as long as man's knowledge of life and its aberrations is as rudimentary as it is to-day. It is thus inevitable that much that is valuable in modern therapeutics is purely empirical, even if rational achievement is frequently the guide to an empiric truth, as it was and still largely is in chemotherapy. But there are also therapeutic measures that have been achieved without any such guidance. The effect of X-rays and radium on cancer cells is a purely empiric discovery; 'shock therapy' by the injection of foreign proteins such as milk is a useful procedure in many inflammatory lesions; the artificial induction of fever has proved a revolutionary step forward in the treatment of the previously incurable condition of general paralysis of the insane; a great field in the treatment of mental disorders was opened up by producing convulsions by drugs or electrical apparatus; pernicious anaemia, previously invariably fatal, is now easily controlled by massive amounts of liver or stomach in the patient's food; blood-transfusion has proved of unexpected benefit in conditions due to other factors than loss of blood; and many other procedures of real, though purely empiric, value are in daily use in the struggle against disease. But no empiric truth remains for long

just that and no more; from a sword in battle it becomes a ploughshare for the tilling of a richer harvest.

8. Surgery

Modern surgery is the unrecognizable offspring of lowly ancestors. The physician of a hundred years ago would understand little of what he would see were he to walk through the wards and laboratories of a modern hospital, but the surgeon of his generation would have the more grievous experience of not being admitted at all to the modern operating theatre, for his presence would be regarded as little less incongruous than that of a witch-doctor. The witch-doctor of antiquity and the surgeon of yesterday would alike fail to understand present-day surgical aims and ritual, and both would bring into the theatre not merely incomprehension, but also danger from their surgical uncleanliness.

Surgery in the modern sense became possible with the introduction of anaesthesia by the middle of the last century and of surgical cleanliness in the two succeeding decades. As long as there was no anaesthesia operations were limited to fantastically rapid procedures consisting largely of amputations and of removal of stone in the bladder. The personal qualities that a surgeon needed were essentially similar to those required of an executioner, and more often than not the surgeon's knife did the work of the executioner's axe. Death from operations was the less

merciful, for it came after the agony of infection of the wound leading to 'surgical fever'. No real advance in surgery was possible until it was recognized that infection in operations was introduced from without; asepsis (surgical cleanliness) is the result of the work of Semmelweiss and Lister, and the development of bacteriology.

Anaesthesia has now developed to such a fine art that neither its dangers nor discomforts need be seriously considered. Nitrous oxide, aether, and chloroform—the three original anaesthetics—are still in use, but a whole range of anaesthetics that can be given by the blood-stream instead of by inhalation, and anaesthetics that do not abolish consciousness but only the sensation of pain (analgesics), are now available. Spinal analgesics injected into the spinal canal abolish sensation over widespread areas, while local analgesics are more limited in their field of action. Medication with sleep-inducing substances before operation has gone far to abolish the last remnant of pre-operative fear. The surgeon can give his undivided attention to the body of his patient; he need not operate under conditions imposed by quivering, sensitive flesh or by the threat of anaesthetic unconsciousness passing into a greater and final oblivion. The surgical speed of a previous age is now a lost acrobatic art. Not the time factor, but gentleness dominates operative technique; the surgeon must not handle but caress the tissues and organs on which he operates.

Asepsis imposes a ritual that goes far deeper than dressing up in white gowns. It is not an exercise in quixotic millinery, but a rigid discipline that aims at isolating the patient from the ubiquitous microbe, for the gentlest operation is a rude breach of the insulating mechanism that the body possesses in its skin and mucous surfaces. The elimination of sepsis from surgery has opened the body cavities to direct approach, enabling the surgeon to see disease processes in the course of actual development instead of as post-mortem appearances, crumbling monuments to extinct life. The opportunity to study the pathology of the living is not the least of the boons that modern surgery has given.

The modern surgeon is not a scavenger but an architect. In its most dramatic form surgical architecture is illustrated by the growing domain of plastic surgery of the face, but many abdominal operations, such as those for gastric and duodenal ulcers, are likewise essays in architecture. Yet surgical architecture is no mere mechanical craft, as over-enthusiastic surgery on the stomach and colon has proved. The surgeon is limited by the fact that his material is a component part of an integrated physiological system, and that his efforts have more than a local significance. The modern surgeon is in fact 'a physician with clever fingers'. Often enough his surgery is of an eliminative kind, as the whole field of cancer surgery shows; sometimes it aims at restoring balance, as in operations on the thyroid gland in Graves' disease or on

the sympathetic nervous system in high blood-pressure; it repairs and reconstructs in operations that overcome the ravages of infantile paralysis and other affections. The surgeon builds better than nature when he restores sight by corneal grafting in congenital or congenitally determined opacification of the cornea, or by diathermy operations for detachment of the retina, a condition that is not infrequently hereditary. Life-saving procedures, such as operations for acute appendicitis and perforated gastric ulcer, or decompression for brain tumour, are still important aspects of surgical practice, but increasingly the surgeon works not for the moment but for the future. To patch and to repair will always be an essential part of his work, but even now the surgeon is no mere apprentice as a plastic artist. Concerned at first with trimming loose ends, the surgeon's task is now to remould the anatomically misshapen or physiologically ill-functioning body.

Men seldom, if ever, control a situation they do not understand. The failure of classical therapeutics arose from this imperative condition of existence, and the triumphs of modern medicine have come from man's recognition of the humble place he occupies in the scheme of things. He no longer demands that the stars in their courses fight his battles, that the waves break only to bring him treasure, that the winds blow only to rain manna. The flowers and herbs in the field are no longer medicines created for his use by a

Providence preoccupied with the care of man; the moon is no longer mere stage property in a drama in which the rest of existence revolves around the self-styled image of God. His newly found humility has taught him to recognize the universe as neither his master nor his slave. In discarding the chains that crippled his mind, man is learning to break the fetters that deform his body.

CHAPTER VIII

Treatment: Collective Measures

1. Epidemics

Were treatment confined to purely individual measures, medicine would represent little more than a brave last stand, frequently foredoomed to failure. Modern medicine has collective duties, not only because it must try to avoid a rearguard engagement, such as the treatment of the sick individual is, but also because man, being a gregarious animal, has herd problems as well as individual problems.

Amidst the calamities that beset social life nothing could be more disastrous than the frequent outbreak of epidemics that swept through communities and sometimes—as in the case of malaria in ancient Greece and the Black Death in the fourteenth century in Europe—completely changed the social structure of the age. From the welter of superstition and terror that such epidemics always unleashed there emerged the beginnings of modern sanitation and the social organization of medicine. In so far as a rational approach to epidemic disease was possible the conception grew up that infectious diseases were miasmas

arising from filth and from contaminated soil and water. The role of an infected individual as a source of infection does not appear to have been clearly recognized: there was thus both helter-skelter flight

FIGURE 22. QUARANTINE
An etching by Daumier.

The cross painted on the house indicated that the house was infected with plague.

from an infected region with its imaginary miasmas and some primitive attempt at isolation in the form of pest-houses and leper colonies for infected individuals. The term malaria, with its implication that the

affection was due to bad air, commemorates an ancient conception.

Until the advent of bacteriology towards the end of the last century the miasmal origin of infectious disease dominated medical thought. Here and there some recognition of the significance of direct spread by infected individuals led to fumbling, ineffective action (Fig. 22). Crass cruelty was the characteristic feature of most such activities, as is shown by the wholesale desertion of the sick, the walling up of houses in which there were affected persons, and the ruthless expulsion of the sick and dying.

By devious and tortuous routes the miasmal conception of infective disease led to various sanitary measures. The indescribable filth in the growing cities of medieval Europe was slowly brought under control. An ordinance of 1283 issued by the City of London prohibited the melting of tallow, with its foul smells, in Chepe; it is possible that the monks of Whitefriars in London, who in 1290 complained of the putrid emanations from the Fleet Ditch as causing the death of many brethren, obtained some redress; in the plague epidemic of 1531-3 in Paris, barbers and surgeons were forbidden to throw the blood produced in their operations into the Seine within the city, while all citizens were prohibited from throwing ordure from the windows. Medieval cities were indeed colourful and odoriferous in more senses than one, and conditions changed but slowly. Latrines under staircases, emptied at intervals by scavengers, were

the acme of sanitation, to be found only in large houses. Cesspools in front of dwellings were a normal feature of life in the first half of the last century (in 1844 one observer counted fifty-three in the basement of Windsor Castle) and the abolition of some 100,000 cesspools in London in the succeeding twenty years is significant of what had still to be achieved in the world's metropolis at such a late date.

War and pestilence were the hard task-masters that evolved a social organization of medicine. Whatever motives inspired the rise of healing temples and the rudiments of public medicine in classical antiquity, medieval Europe had to develop such services under the lash of adversity. There may have been some little charity, but Dives feared for himself rather than felt for Lazarus. The pest-house and the leper-house were a sort of social insurance; 'the myserable people lyeing in the streete, offending every clene person passyng by the way w^t^ theyre fylthye and nastye savors', called forth in medieval breasts not the tenderness of mercy but the pugnacity of self-preservation. A salaried medical service developed overnight in plague-maddened Marseilles in 1720, when the city fathers ordained that physicians should not demand any fee of the sick, but have salaries from the city, and be given overalls of oiled cloth and chairs for their more easy conveyance; even the principle of compulsion was applied, physicians who had fled the city being ordered to return on pain of expulsion from the Faculty. In this criss-cross of futile flight from

pestilence and equally futile attemps at bottling it up, quarantine emerged as a precautionary measure against individuals and ships. The rigidly fixed forty days of the quarantine, as originally practised, implies that the measure had more theological than scientific sanction.

2. Sanitation

If for nothing else, the second half of the nineteenth century will ever be memorable for its massive advances in sanitation. Centuries of halting effort came to fruition in a new conception of individual and collective cleanliness. That conception developed almost inevitably from the danger of epidemics that the rapidly growing means of communications brought with them. In a shrinking world cholera, plague, and typhoid could march in seven-league boots, while in a world throbbing with movement the cesspool came to be regarded as a spouting well of pestilence rather than as an unlovely private spittoon, protected by the rights of property. Sanitation and health had emerged as a public policy of an overriding character, as a British Prime Minister declared in introducing the 1875 Public Health Act: *Sanitas sanitatum, omnia sanitas.* That some should have sneered at the Bill—the Magna Charta of public health—as an Act of Sewerage only illustrates that the fools, like the poor, are always with us.

By the middle of the last century the blind gropings of generations had seized upon sanitation, quarantine,

and the beginnings of an organized medical service, including hospitals for the sick. These agencies, harnessed by the then newly rising science of bacteriology, have since developed into a force that has eliminated infectious disease and much else that is deleterious.

In England the supply of pure drinking water brought cholera and typhoid under control before bacteriology showed that these were generally water-borne infections. Such diminution in overcrowding and filth as sanitation had brought about made typhus fever a rare disease before it was known to be carried by the louse. Plague had ceased to decimate the country long before it was recognized as a flea-borne scourge.

3. Bacteriological control

But these were uncertain conquests till bacteriology, by identifying definite organisms as the causes of a variety of infections, laid bare at one stroke a clear line of advance. It was no longer a question of sanitation in general; the life-history of the causal organism could now be studied and the ways by which it spreads—whether by direct contact, air-currents, water, contaminated food, or by intermediate hosts like fleas and mosquitoes—could be established. Where before, man had fumbled, advancing blindly here and fleeing in terror there, a world—his own world—lay exposed for systematic conquest.

For civilized communities epidemics like those of

typhoid, typhus, cholera, plague, malaria, yellow fever, and many other infections are no longer a normal feature of life. Under exceptional conditions a minor epidemic may occur here and there, but the failure in sanitation responsible for it can quickly be remedied by decisive and purposive action.

The elimination of epidemics from organized social life is largely a question of disrupting the conditions under which the infecting organism can gain access to man. In the case of typhoid fever the bacillus is transferred from patient to patient chiefly through excreta (faeces and urine) of an infected individual contaminating drinking water, or more rarely food. The problem therefore resolves itself into the sanitary problem of the disposal of ordure and the endless vigilance that has to be exercised in supplying pure water to communities. Occasionally an epidemic may start from shell-fish and mussels grown in infected water, and this illustrates the multiplicity of ways in which organisms may gain access to man. Generally speaking, there is little difficulty in checking infections carried bij water and food, though the occurrence of tuberculosis from infected milk shows how much still remains to be done in relatively simple problems in the prevention of the spread of infection. A more difficult problem is the prevention of infection by microbes that are carried by active living agents. It required much painstaking and brilliant work before it was realized that the malaria parasite does not attack man directly, but has to develop to a definite

stage within the mosquito before it can infect man. In fact the parasite, the mosquito, and man, constitute a unity, and the elimination of malaria meant the elimination of either the parasite or the mosquito. In practice the destruction of mosquito life, by draining swamps and other measures, is a relatively simple procedure. Yellow fever presented a similar, though somewhat simpler problem. Here infection is transmitted from patient to patient through the mosquito, which acts as a carrier rather than as an incubator of yellow fever virus, and had not this particular mosquito been overcome there would have been no Panama Canal.

The history of typhus has been described as the history of human misery, for typhus is the outstanding example of a whole host of infections prevalent wherever poverty reaches its most degrading levels. These diseases are louse-borne (rickettsias), the bite of the louse transferring infection from one individual to another. The sum total of louse-borne disease—virulent epidemics or minor maladies—is a sardonic reminder to man that it shall profit him little if he conquer the whole world but not himself.

Air-borne infections, spread by the sneezing and coughing of affected individuals, present a considerably more difficult problem than infections carried by agents more amenable to control than is the air. Tuberculosis, diphtheria, scarlet fever, measles, chickenpox and the ordinary influenzal cold can all be conveyed by the air, though usually air-borne infec-

tion is only one of the ways in which a particular disease can be spread. In the control of infection general sanitary measures are therefore helpful, as is isolation of the infected individual, for this helps to prevent the spread of the infection by air. Dilution of the infecting medium by proper ventilation is also useful and fully justifies the spaciousness of fever hospitals. None the less, airborne infection presents a difficult problem and much of the residue of infective disease in our day centres around this difficulty. Measles, scarlet fever, diphtheria, chicken-pox, and the ordinary influenzal cold illustrate the persistence of a problem reminiscent of the miasmas of our ancestors.

The successes obtained in the conquest of infectious disease have come largely not from the extermination of the infecting organism, but from the control of the means by which it reaches man. The means may be inanimate, such as water and food, or animate such as mosquitoes; in either case they can be controlled. Where the contacts between man and the microbe cannot be effectively broken, as in air-borne infection, successful action lies not in the as yet impossible task of exterminating the microbe, but in building up man's resistance to it.

The empiric discovery in the eighteenth century of vaccination against smallpox is by itself one of the high-water marks of human history, for it introduced protection against a disease that counted its victims in millions century by century. Vaccination remained

an isolated triumph till the advent of bacteriology showed that a similar procedure could be used for other infections, and to-day the induction of sham attacks of infections to stimulate the production by the body of protective antibodies against the disease is a daily practice. It is employed in some easily controlled affections like typhoid fever when there is a danger that sanitary measures may break down: thus it was used extensively and successfully in both the first and second world wars in campaigns and regions where it was feared that typhoid might break out in spite of all sanitary precautions. It finds a direct application in daily life in the active immunization of children against diphtheria. Where immunization has been applied extensively, as in New York and many other towns, diphtheria has been abolished as one of the major killing diseases (Fig. 23). The incidence of diphtheria has declined strikingly, and such cases of the affections as occur run a mild course. Scarlet fever, too, is being brought under control, and there is a hopeful prospect that measles and whooping-cough, the remaining killing diseases of child life, will be banished soon.

As between an isolated case of disease induced by microbial life and an epidemic or pandemic, the determining factors are not only the possibility of spread of the infection but also the presence of a population susceptible to the infection. In affections like yellow fever, typhoid fever, and largely also in diphtheria,

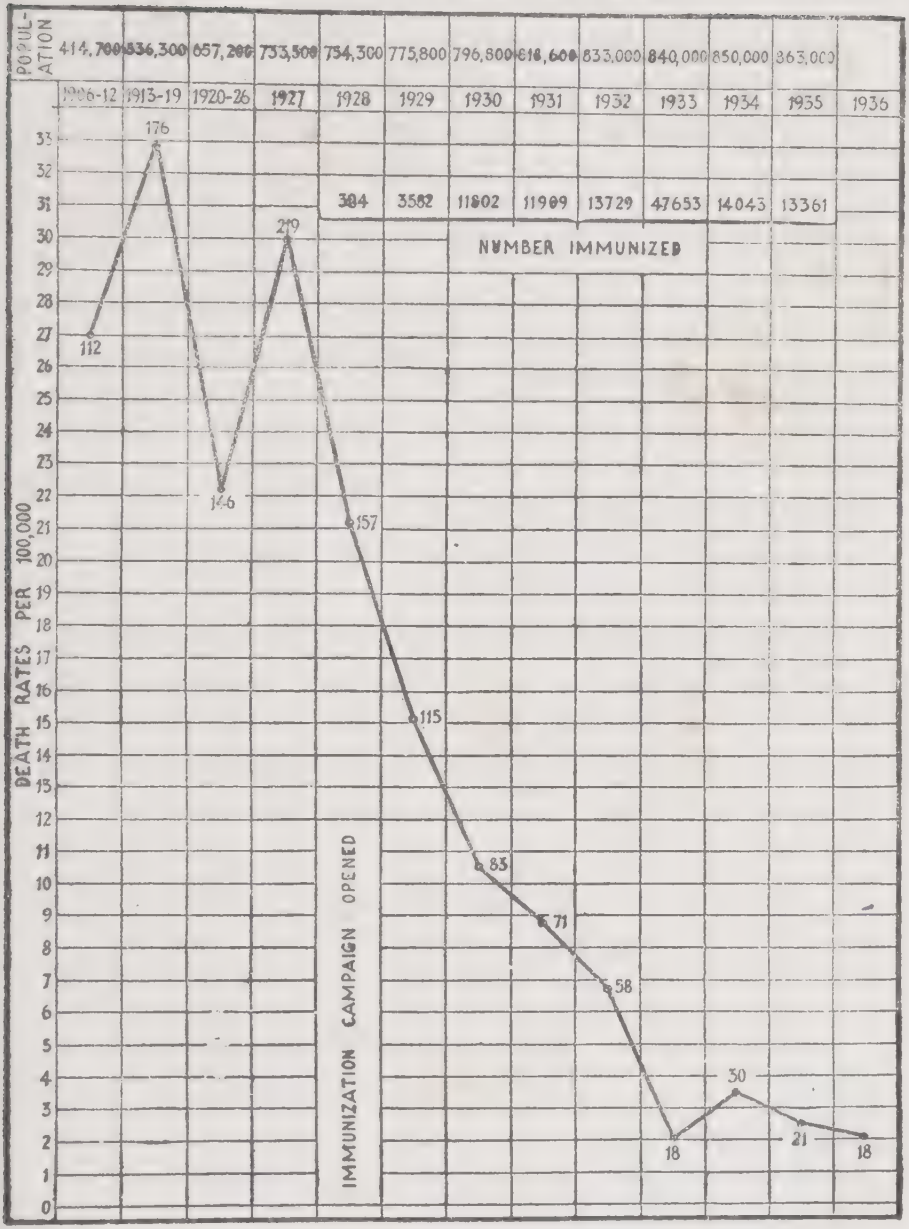


FIGURE 23. DIPHTHERIA MORTALITY RATE IN MONTREAL, 1906-37

Immunization campaign was opened in 1928. The figures at each point in the graph indicate the yearly number of deaths from diphtheria in Montreal.

one attack makes the patient immune against a second attack : the body has produced a defensive agency to withstand the particular microbe. The presence or absence of this defensive agency in, say, diphtheria, can readily be demonstrated: in a person who is resistant to diphtheria a controlled amount of diphtheria toxin injected beneath the skin fails to induce any local reaction, but in a susceptible individual the toxin produces a local reddening. This is the basis of the Schick test for distinguishing susceptible persons from the non-susceptible. Similar tests have been elaborated for other infections, and it assumed that in the common infective diseases the non-susceptible are people who have experienced a mild, unnoticed (subclinical) attack of the disease. The object of immunization is to induce such subclinical attacks in the susceptible population (shown susceptible by a positive skin test) by injecting a controlled amount of toxin. In diphtheria immunization, toxin, suitably prepared to reduce the toxicity to a minimum (toxoid), injected at one sitting or at three spaced intervals, generally converts a diphtheria-susceptible person into one no longer susceptible—an achievement that is shown valid both by the failure to obtain a positive skin test after the injection, and by the absence of diphtheria in such protected individuals should they become exposed later to the infection either in an epidemic or otherwise.

Tuberculosis illustrates both the possibilities and limitations of procedures derived from bacteriology.

The incidence of tuberculosis can be drastically lowered by the elimination of tubercle-contaminated milk and meat; sanitary measures can do much to overcome airborne spread of infection; but any direct attack on the tubercle bacillus is only now becoming

FIGURE 24. A ROOM IN THE HOTEL DIEU, A HOSPITAL IN PARIS

From a woodcut of the sixteenth century.

A report on conditions in 1788 relates that the hospital had 1,220 beds, each bed containing from four to six patients (sometimes regardless of sex or disease). Over 800 patients lay on piles of straw on the floors of passages. The stench was so bad that the attendants went about with sponges, soaked with vinegar, before their faces.

possible by the use of streptomycin, whilst attempts to build up the individual's resistance by stimulating the production of protective substances in the body by injecting tubercle toxin or dead bacteria have been distinctly disappointing. (Judgment has

yet to be suspended on the method of immunization by attenuated tubercle bacilli *(Bacillus Calmette-Guerin)* extensively used in France in young children, and the still more recent method of inoculation with the vole bacillus, an organism closely allied to the bacillus of human tuberculosis. This organism readily induces a modified (and fatal) form of tuberculosis in voles (water rats); it is almost innocuous to man, in whom, however, it would seem to produce a marked defensive reaction to tuberculosis: the principle involved is the same as the protection against smallpox by vaccination with the allied but milder condition of cow-pox).

Man's struggle against ubiquitous microbial life harmful to himself is an epic battle in which the trophies are millions of lives saved. Most of the major epidemic diseases are no longer the formidable agents of destruction they were in the past. The organisms causing them are indeed still with us, but man can live secure in a world in which he has cut all the roads on which they can travel, and has built an impenetrable defence within himself against any organisms that do reach him. That the blocking of the roads of disaster and the building of internal defence are as yet incomplete is not an admission of failure but an incentive to further effort.

4. Hospitals as centres for team work

In the Middle Ages the hospital had a simple function: it was the gateway to death (Fig. 24). At its

best it was the medieval form of euthanasia, at its worst a social cesspool where derelict humanity was robbed of a flickering last hope and drowned in its own despair. To the modern hospital problems of death are incidental. The modern hospital is at one and the same time a haven for the sick, a seismograph recording tremors in the social organization of health, a clearing house of pathological currency, and above all a laboratory where the sick are studied for their own sakes and the dead for the benefit of the living. Far from acting as a gateway to death, it is a window opening on the tumultuous scene of life.

In that vista there are no lines of demarcation between health and disease. The hospital service has to provide for that which is clearly abnormal: it must ease the pains of the dying, it must provide anodynes for the suffering, it must mend the maimed, and stem the ravages of disease. It serves all these purposes, but in serving them it merely performs duties that medicine has performed throughout the ages, according to its dim contemporary light. What distinguishes the modern hospital from its predecessors is not so much its greater efficiency but the qualitative difference of its work. The modern hospital must be regarded first and foremost as a centre for diagnosis. It is true that much of the treatment a hospital offers is so highly co-ordinated that it can be provided only by an organized institution. This applies to most surgical procedures and to some forms of medical treatment; but the essential feature of a hospital is

the provision of opportunities for team-work : the co-ordinated study by many minds and many disciplines of those aspects of disease that are beyond elucidation by any one single approach. Diagnosis serves the individual patient in understanding his own difficulties and paving the way for effective action, where it is possible. But the social significance of early and accurate diagnosis lies in extending the boundaries of knowledge on that hazy borderline that separates the healthy from the diseased. The modern hospital need not often compete with less organized institutions for the actual treatment of a patient: when necessary even a major operation can be successfully performed in rather primitive conditions, but only the highly organized modern hospital can hope to explore and lay bare the unknown. Early diagnosis carries not only a deeper knowledge of the factors causing disturbance in the balance of health, but also far greater possibilities for satisfactory readjustment before the process has gone too far.

5. Co-ordinated services

Historically the hospital has also this immense significance : it was the beginning of co-ordinated medical services. The modern hospital is but the hub around which revolves a whole system of agencies that will ultimately emerge into a coherent social organization in which the care of the sick will be a subsidiary consideration. Just as the control of outbreaks of

typhoid is no longer part of the normal routine duties of a medical officer of health, so in a coherent health service the treatment of the sick will be the rectification of the occasional accident that should not happen. The agencies that are emerging are many in number and varied in character : research institutes, national health insurance schemes whereby medical services are available free when they are needed, school medical services for the periodic inspection of school children and the detection of early disease or conditions likely to produce disease, industrial medical services in some factories, health centres for filling gaps in various national schemes, ante-natal clinics for expectant mothers, infant welfare centres, child guidance clinics, and a whole host of loosely connected services, sometimes statutory and frequently voluntary, sometimes overlapping and more frequently leaving essential fields of activity untouched. In Great Britain, there is now at last the prospect of the co-ordination of all such agencies into a coherent national health service. Negative features, such as the window tax in force till 1803, have become unthinkable in the mental atmosphere in which hygiene has become an individual and social good.

6. Some results

During the past hundred years, though the mystery of life has eluded him, man has gained a glimpse of the secret of living. Some factors stand out in that majestic progress, but the whole achievement has

been made up by a multitude of forces all of which are still in the process of development. The gains have been far from uniform in different countries, but as an indication of what these forces are capable of achieving, the advances in any highly organized state are sufficient.

The death-rate in England and Wales was 20.6 per

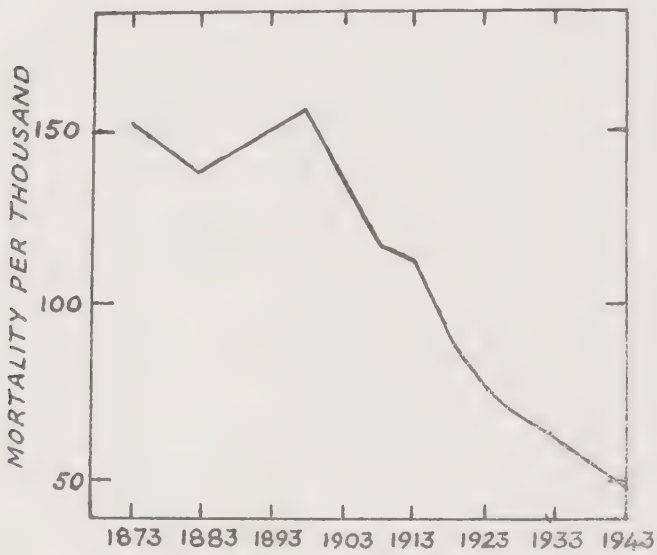


FIGURE 25. INFANT MORTALITY RATE 1873-1943
The rate has declined to about one-third.

1,000 living in 1868; in 1945 it was 11.4. In the same period the infant mortality declined from 155 to 46 (Fig. 25). In 1854 the expectation of life at birth was 39.9 years for males and 41.85 for females; in 1935-7 it was 60.17 and 64.35 years respectively. Cholera,

which appeared four times between 1831 and 1868 and claimed a quarter of a million deaths in the epidemic of 1848-54, has disappeared. Typhoid fever, which in 1871-5 killed 371 out of every million persons living, has declined to possessing a mortality rate of 1 in-1944 and the rate of smallpox has declined from 392 to nil. In 1861-70 the death-rate for scarlet fever per million living (under the age of fifteen years) was 2,617; it has steadily fallen to 9 by 1944; in diph-

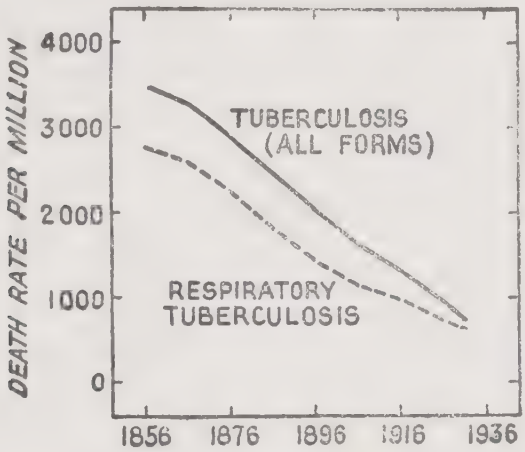


FIGURE 26. DECLINE OF TUBERCULOSIS

Standardized death-rate from tuberculosis (all forms) and from respiratory tuberculosis 1856-1936.

The decline, though marked, is not so extensive as with many acute infections, such as typhoid fever.

theria the decline was from 1,148 to 92; in whooping-cough from 1,475 to 121, in measles from 1,221 to 28. A less drastic decline is recorded for tuberculosis: from 3,638 deaths per millon living in 1851-5 to 782 in 1931-5 (Fig. 26).

The decline in mortality reflects a much more extensive decline in morbidity, and has reduced to smaller proportions one of the causes of human misery: poverty arising from ill-health. In 1836, at the height of the harshest period of English Poor Law administration, one-fifth of the total recipients of poor relief in London were ill with fever, the incidence of illness in some districts being 50 per cent and even 87 per cent in one particular area (Saint George the Martyr). A measure of the positive gains in health is given by school returns. In the London County Council schools 39.5 per cent of children had parasitic skin affections in 1912; by 1937 the incidence was reduced to 2.6 per cent. Ringworm of the scalp declined from 6,214 cases in 1911 to 78 in 1937. In 1926, 2 per cent of children in these schools suffered from heart disease acquired from acute rheumatism; by 1936 the incidence had declined to 0.8 per cent. In Leeds schools during the twenty years 1911-31 the average height of boys aged twelve years attending elementary schools increased from 4 feet 4 ins. to 4 feet 7 ins. and weight from 63.5 pounds to 74.4 pounds. In London the height of a child of five and a half years is to-day much the same as that of a child of six and a half years of a generation ago. A whole host of affections, like trachoma, that previously constituted a permanent handicap have been stamped out from child life. The striking decline in partial deafness in childhood enables the development of an adult population with a keener sense of the richness of life; crippling defects

no longer run their relentless course, and the examination of recruits in the second world war has revealed that medically at any rate the world is a healthier place than it was in 1914.

Some little philanthropy, much more panic, and very much less planning, have determined the growth of organized medicine. Panic no longer dictates its actions, and planning is changing medicine from limited individual action into a social function with limitless prospects.

CHAPTER IX

Social Achievements and Social Frustrations

1. The demographic background of medicine

A previous generation regarded cities as graveyards of mankind. The health problems that were raised by the monstrous growth of towns during the last century forcibly illustrate the ever-changing character of the immediate duties of medicine in a changing world.

That cities as such are no longer graveyards of mankind is true, but none the less morbidity and mortality are still greater in urban areas than in rural districts and the intricate series of factors responsible for this indicate a complexity of affairs beyond the capacity of medicine fashioned and serving as an isolated activity.

In the England of two hundred years ago three out of four children died before reaching the age of five years. Were there to-day anything approaching such a wastage of child-life a rapid depopulation would occur, for the present low birth-rate demands the strictest preservation of child-life; and if the prevail-

ing trend in population statistics continues this preservation will become an ever more pressing social necessity. Even with the strictest preservation Western Europe will become at first a stagnant society

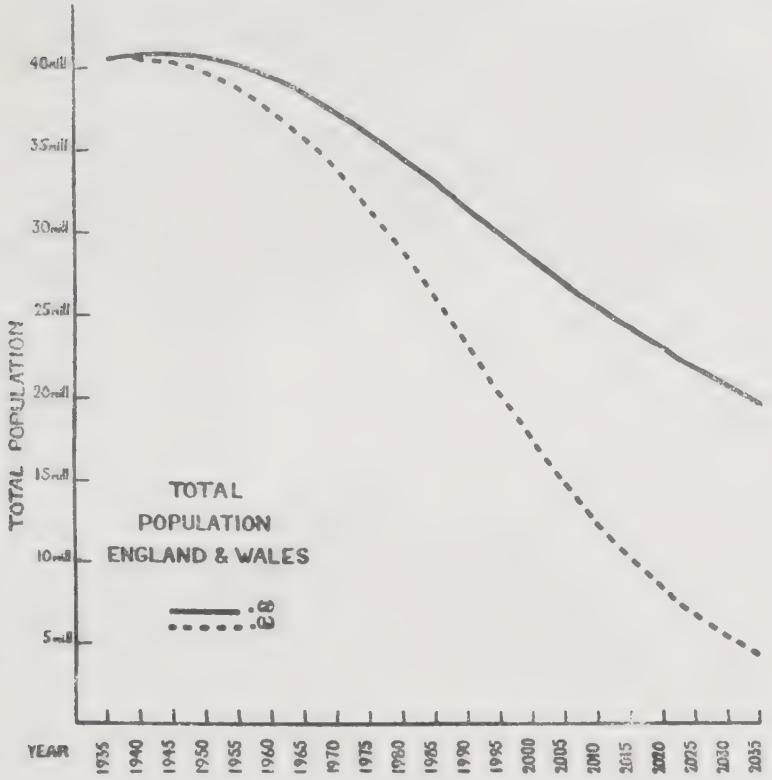


FIGURE 27. ESTIMATES OF THE LIKELY DECLINE OF POPULATION IN ENGLAND AND WALES

Two estimates (a and b) by different methods of the likely trend in population for 1935-2035.

with an undue proportion of middle-aged and aged people, and subsequently a dwindling community (Figs. 27 & 28). Racial suicide is not a sudden but a culminating act.

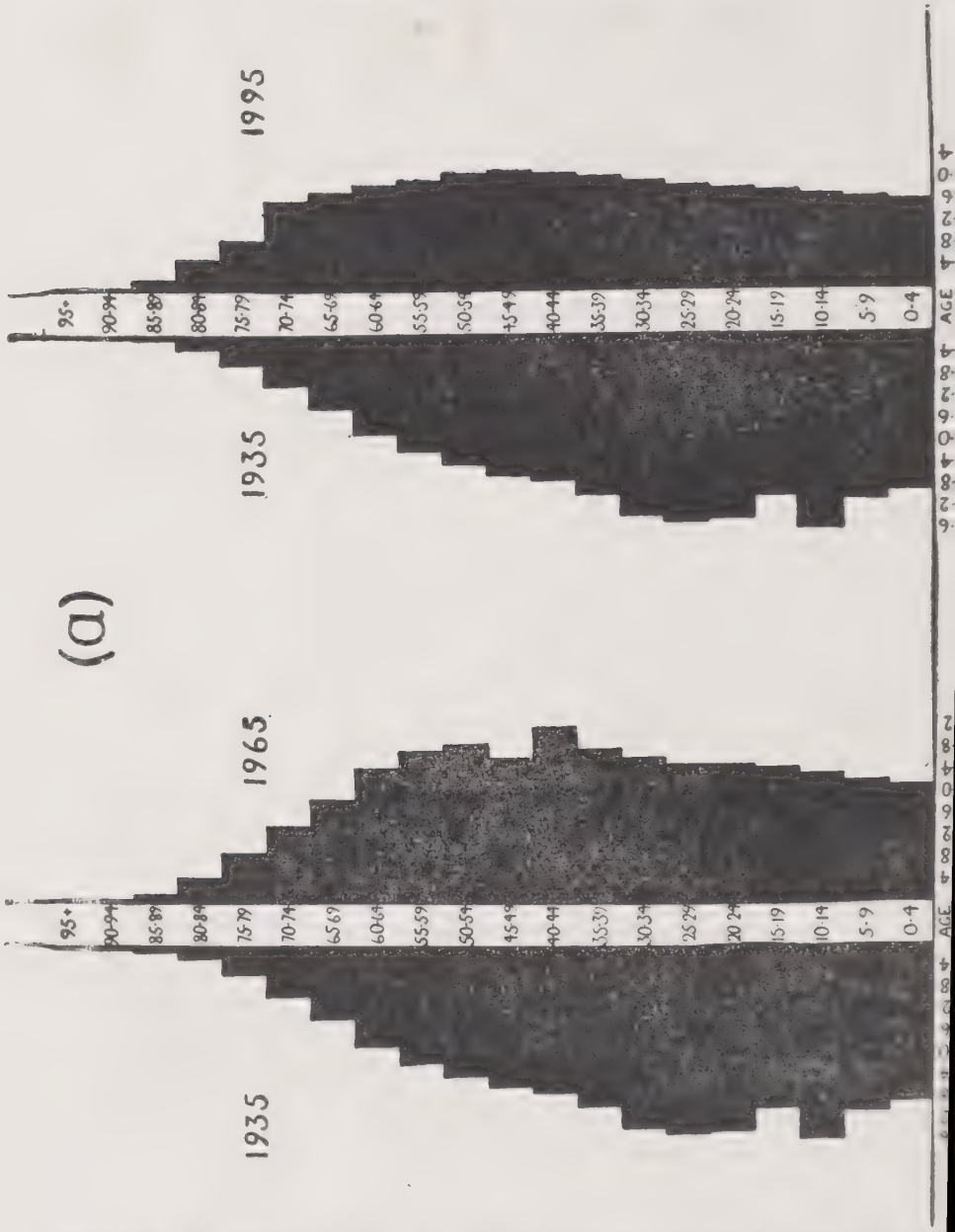
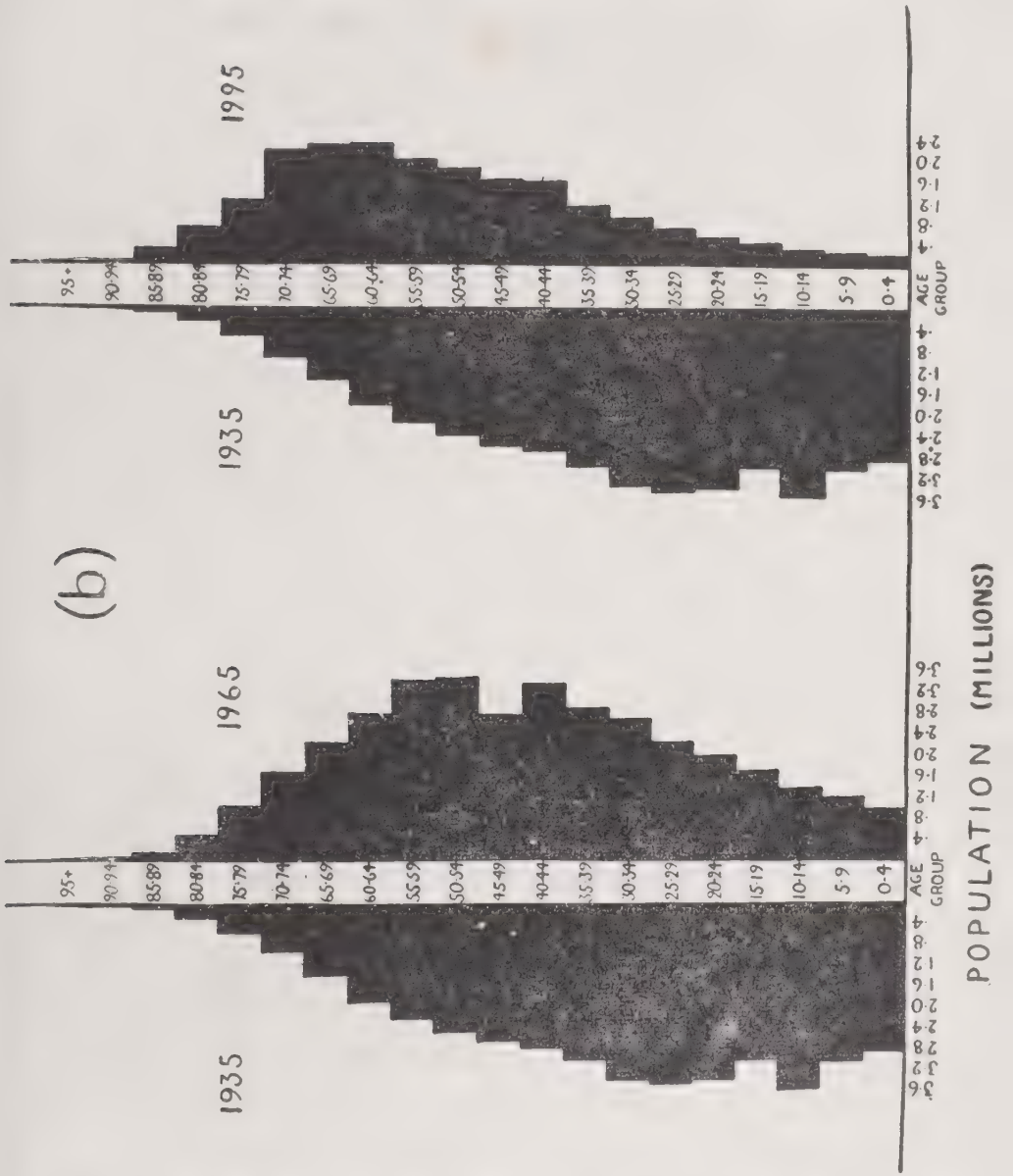


FIGURE 28. ESTIMATES OF THE LIKELY AGE DISTRIBUTION

(a) Actual age distribution of population of England and Wales in 1935 with computed age distribution in 1965 and 1995 based on estimate (a) of total-population in Figure 27.



IN THE DECLINING POPULATION OF ENGLAND AND WALES

(b) Corresponding values to those in (a) based on estimate (b) in Figure 27.

Both estimates indicate a striking decline in the numbers of children and young adults.

The reproductive rate of a particular generation is determined by the number of potential mothers it produces to perpetuate the race. In Western and Northern Europe this number has already declined below the point necessary for a stationary population: a hundred mothers now reproduce only ninety-three daughters. In England and Wales there were nearly a million less children (aged up to fourteen years) at the census of 1931 than at the census of 1921 and there was a further similar fall between 1931 and 1941. The declining birth-rate hides a considerable social disparity: the decline is unequal for different sections of the population. It is marked for the well-to-do and professional classes, and not so heavy for the poorer sections of the community: homes where young life can develop to best advantage contain fewest children.

Any saving of infant life is thus a social need of first importance. While the decline of infant mortality from 155 per 1,000 births in 1868 to 46 in 1945 implies the saving of many hundred thousands of lives, the rate of 34 recorded in 1948 indicates that much more is still possible. That there is, however, a definite limitation in improvement from measures adopted today is shown by the fact that the incidence of death in infants in the first day of life has hardly changed during the past thirty years. The mortality rate for infants two to four weeks old has fallen continuously during the century and has been halved, and for infants over one month has been reduced by 60 to 70

per cent, but something like a fifth of the total deaths of infants under one year are still concentrated in the first day of life, and this mortality has remained unaffected. Obviously a new approach is necessary in ante-natal care and in the care of the new-born.

The death rate in adult life has declined considerably during the present century, by 25 to 40 per cent for the different age groups between fifteen and forty years. Yet the two main factors of death in the early twenties—tuberculosis for women and accidents for men—have shown no appreciable reduction. Here, too, reliance on the cumulative effect of measures already in operation is leading to wastage of young life—all the more regrettable, as it can be ill-afforded socially.

In escaping from the burdens imposed on it by a dependent childhood and in wasting young life society is loading up for itself an inevitable burden of decrepit age.

2. The social background

The observation that cities are the graveyards of mankind was a half-truth, in so far as no distinction was made between the amenities and the mode of living in cities. The comparative mortality rates of town and county still weigh heavily against towns, though not to such an extent as even in the recent past. In 1911-14 the average excess of deaths in English country boroughs over rural districts was 46 per cent; twenty years later it was 25 per cent. Such figures reflect the complex tangle of the effect of occupation,

economic status, overcrowding, malnutrition, facilities for treatment, and the sum total of the factors that make towards social differentiation.

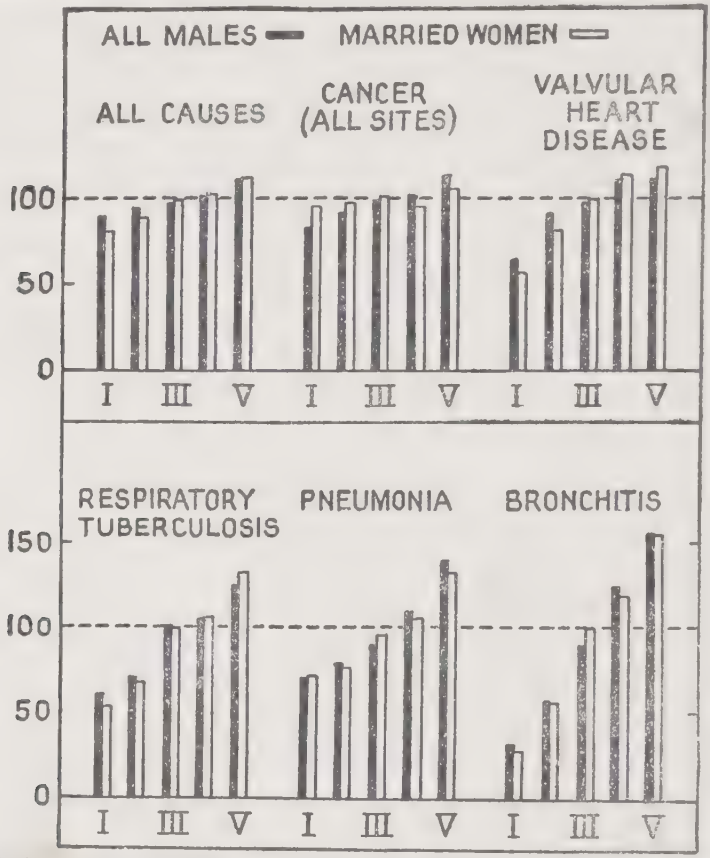


FIGURE 29. GENERAL MORTALITY BY SOCIAL CLASS

Mortality of men and married women aged 20-65 years for various causes according to social class. 1930-2.

Mortality rates vary immensely for different sections of the population (Fig. 29). For England and Wales in 1921-3 the total mortality rate for men between the ages of twenty and sixty-five years was 48 per cent higher in unskilled labourers than in the well-to-do and professional classes; in 1930-2 this

excess had declined by half (Classes V and I in the Registrar-General's classification). The excess of mortality is not uniform for all causes of death: it is most marked in respiratory diseases, including pulmonary tuberculosis, and in all these differences skilled labourers occupy a position midway between the two other classes. In broad outline the lower the economic status the higher the total mortality, this increase being seen throughout the various age-groups; there is a greater incidence of some affections such as diabetes in the well-to-do, but whereas the well-to-do are afflicted by a limited group of diseases in advanced age, the great excess of respiratory diseases in the poorer sections of the community operates throughout active life and not least in those years when life is most vigorous.

The excess of morbidity and mortality in the poor as a mass is not due to mystical causes, like 'poor stock'. This is obvious from the facts that not all affections fall with the same heavier incidence on the poor, and that the excessive mortality rate is declining steeply under public health measures. The poor sicken and die from the same causes as the well-to-do. They react not differently but more readily, and tangible factors are responsible for the immense loss of health and life that goes on daily. Faulty nutrition and overcrowding will induce in a herd of experimental animals the disease phenomena reflected by human statistics. Respiratory affections can be made rampant in a rat colony by feeding which corresponds to the

imbalanced diets of the poor, and mortality statistics in India, with its great variety of dietetic imbalances, bear out the paramount influence of faulty diet in determining the development of infections, particularly of the respiratory tract. Overcrowding, with its dust and dirt and its lack of fresh air and sunshine, concentrates factors that operate on a favourable soil

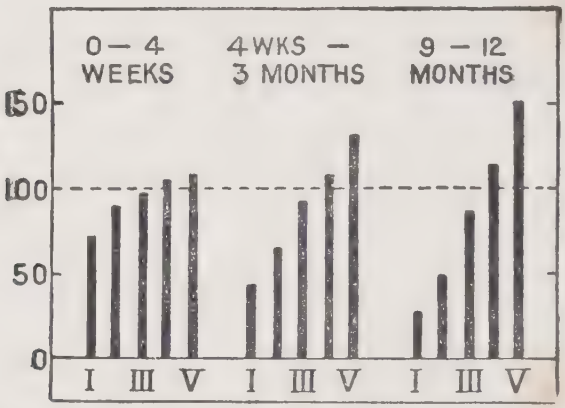


FIGURE 30. INFANTILE MORTALITY BY SOCIAL CLASS

Mortality of infants of various ages according to the social class of the fathers, 1930-2.

in the undernourished. Thus no single factor of the vicious circle of poverty is an exclusive cause. The pre-war evidence from Stockton-on-Tees, where the rehousing of a slum population on to a corporation estate led to greater morbidity and mortality from the fact that the higher rents meant less money for food, forcibly illustrates that poverty, like all reality is indivisible.

The influence of social conditions on mortality is strikingly seen in infantile mortality (Fig. 28). The

rate for the total population in 1930-2 was 62 per 1,000 children born: it was 33 for infants of the well-to-do, 77 for those of unskilled labourers, and 58 for skilled artisans (Classes I, V, and III of Registrar-General). In terms of percentages it was 100 for the total population, 53 for Class I, 125 for Class V, and 94 for the intermediate Class III. Injury at birth and congenital abnormalities as causes of death showed the same incidence in all sections of the community, but preventable conditions and conditions amenable to treatment showed vast differences: they were lowest in Class I and rose steadily within the five social divisions to extreme figures in Class V. Congenital debility had a rate of 14 per 10,000 in Class I and 38 in Class V; whooping-cough a rate of 3 against 27; bronchitis and pneumonia 28 against 188, and diarrhoea and enteritis 20 against 79. Mortality in the second year of life shows the same trend for these two contrasted classes: the rates for measles were 2.5 against 46.9, for whooping-cough 2.8 against 20.9, diphtheria 1.3 against 5.5, tuberculosis 6.9 against 15.0, bronchitis and pneumonia 12.8 against 86.1, diarrhoea and enteritis 2.8 against 11.48.

The relationship between overcrowding and infantile mortality is seen from the great infantile mortality rate in overcrowded areas, and the low rate in least crowded districts. Thus in Sunderland working-class families show overcrowding, as defined officially, to the appalling extent of 20.6 per cent; in 1935 its infantile mortality rate was 92 per 1,000, against

57 for England and Wales, while Bournemouth, largely residential, with overcrowding of only 0.3 per cent, had an infantile mortality rate of 40. In a large slum area of Birmingham the infantile mortality rate in 1925 was 171 against 89 in fair artisan districts. In Welwyn Garden City it was 25 against 62 for England and Wales and 120 for the slums of Manchester.

The intricate interaction of the various factors of poverty is illustrated by the tuberculosis mortality in young women. In contrast to the decline observed in other sections of the community, deaths from tuberculosis have on the whole remained at a stationary level, especially in the metropolitan and county boroughs, more particularly in those with the worst housing. The rather sharp check that took place in the improvement of the standard of living about 1900 and the increasing proportion of young women entering industrial occupations in overcrowded areas are the two factors that militate against the expected decline from improved sanitation and social services. The wastage of life from tuberculosis in young women shows only too clearly that such improvements as occur in mortality rates are due to the elimination of specific deleterious factors; where in the medley of interacting social forces factors favourable for the propagation of disease are left untouched or created anew, the consequences are inevitable and inexorable.

The significance of tuberculosis in national welfare is apparent from the fact that even in a relatively non-tuberculous country like England the disease

accounts for more deaths in the population aged ten to forty years than any other one affection; and the role of poverty in this slaughter is attested by a host of correlations between the different factors of poverty and the ravages of the disease. Tuberculosis was rife on the Continent in the famine years during and following the two world wars : in two occupied industrial towns in Northern France it rose by 101 per cent and 183 per cent respectively during 1914-18; in the Netherlands the mortality rate in 1944 was double that of 1939. In the British Isles the morbidity and mortality follow closely the social distinctions that operate on the infantile mortality rate: apart from nutrition, housing is an essential factor—in Glasgow in 1932 the death-rate per 1,000 cases was 1.4 in one-roomed apartments, 1.1 in two-roomed houses, 0.72 in three-roomed and 0.46 in four-roomed houses.

3. Environment and health

Good physique—the basis of a healthy body—and good nutrition are closely related. Hereditary factors are important, but in most instances of poor physique environmental factors are clearly discernible. In a relatively small series in Newcastle it was found that both for height and weight of children, the social status of the parents was all significant (47 per cent of working-class children as against 4.8 per cent of middle-class children were below normal height, 1.7 per cent and 25 per cent were above normal for the two respective groups; 55.2 per cent and 12.9 per cent

respectively were below normal weight). At one public school boys at thirteen were 2.4 inches taller than boys of the same age in council schools and 3.8 inches taller at seventeen than boys of that age in gainful occupations: that such a difference is not all due to heredity is clear from nutrition experiments on animals and from controlled observations in schools. At one industrial school boys fed on the normal school diet grew at the rate of 1.84 inches per year, while those receiving extra milk grew at the rate of 2.6 inches a year. A 20 per cent increase in the rate of growth was observed in an extensive experiment in Scotland for children receiving extra milk for seven months. Children born in Berlin in 1918 and entering school in 1925 were appreciably smaller than those entering school in 1933. In Glasgow it is officially reported that 'the average heights and weights of children bear a direct relationship to the size of the houses occupied by the families; that is to say, the smaller children come from the smaller houses, and the larger children come from the larger houses'. While comparative data on nutrition of children are difficult to establish, it is significant that in 1935 Jarrow, a depressed area, reported 22.9 per cent of 'slightly subnormal' and 6.7 per cent 'bad' state of nutrition in children against 10.7 and 0.7 per cent for England and Wales. That income is the determining factor in nutrition has been clearly established by Lord Boyd-Orr in investigations prior to the second world war. Before the prevailing world shortage of

food had become apparent, Boyd-Orr estimated that for economic reasons half the population of the British Isles was living on a diet subnormal, partly in quantity but mainly in quality. It was only in families where the income per head was over twenty shillings a week and ten shillings could be spent on food that diet became adequate. Other evidence suggests that even this was an underestimate.

4. Overcrowding and nutritional deficiencies

Overcrowding and nutritional deficiency are the social leeches that drain the life-blood of whole populations. Standards for normal density of population and normal nutrition cannot be clearly established, though the effects of low standards are reflected readily enough in high morbidity and mortality. By the relatively unexacting official standard of overcrowding 3.8 per cent of families in England and Wales were living in overcrowded conditions in 1936; by a slightly more stringent standard the level was nearer 10 per cent. Even by the official standards overcrowding was extensive in many districts: in 17.2 per cent working-class families in Shoreditch, and 25.2 per cent in Hebburn. In Scotland the 1931 census showed that 44 per cent of the population were living in houses of one and two apartments, and 15 per cent were living in rooms housing four or more persons. On official standards of overcrowding working-class families in 1936 showed a rate of 40.4 per cent at Motherwell, 40.9 per

cent at Coatbridge, 42.1 per cent at Port Glasgow, 44.9 per cent at Clydebank; many mining towns and villages throughout Scotland were little better.

Standards for nutrition are also difficult, but nutritional anaemia is a useful guide. In Aberdeen Boyd-Orr found that 50 per cent of women in the lower economic groups (families with less than twenty shillings per head per week) showed laboratory evidence of anaemia, 15 per cent being severely anaemic. In London less than 30 per cent of a similar group of women had a normal haemoglobin level. That nutritional anaemia in a pregnant woman is transmitted to the offspring makes this finding all the more perturbing from the point of view of national health. In a group of children under school age 23 per cent of the poorest class were anaemic, against not a single case in children of the well-to-do class.

5. Occupational disease and mortality

What the Enclosure Acts had begun, by dispossessing the people of their land, the industrial revolution completed by driving them into the towns. By 1851 England was becoming an urban country, the census figures giving the urban population as 50.2 per cent, and this percentage increased steadily to around 80.0 for 1911-31. The stratification of society as reflected by the Registrar-General's five social classes, each with characteristic mortality rates, is the outstanding fact governing health and disease. Social level rather than actual occupation determines the

mode of life and death, as is apparent from a comparison of male and female mortality. In each of the five social classes female mortality, though smaller than the male rate, follows closely the rate established for the class and not for women as a whole, in spite of the fact that the occupation of women in each class is markedly different from that of the men in the group. Yet the fact that male mortality is higher in each social class and at all ages, but more particularly between thirty-five and fifty-five, when most men and but relatively few women are in gainful occupations, suggests that the excess of male mortality is occupational in origin. If the mortality statistics for society as a whole primarily incriminate our tenement dwellings, with their lack of air and food, our factories and mines also exact a toll.

In all the five social groups there are marked differences in mortality according to occupation. In Class 1 (professional, etc.), in which the mortality rate is considerably lower than for the other social groups, looking after the physical well-being of the people is seen to be a more exhaustive task than guarding their monetary stability: the mortality rate for doctors is 6 per cent higher than for the group as a whole, and 40 per cent higher than for bank officials, with their sedentary and well-regulated mode of life. But the social structure of society is such that Class III (skilled workers) is by far the largest, making 49 per cent all males, and Class IV, the semi-skilled, comprises 18 per cent. It is in these two classes,

constituting 67 per cent of the total male population, that the lethal effect of some occupations is clearly apparent. The low social position of these classes does in the first place determine a high mortality rate, but some occupations, such as various forms of agricultural activities, are relatively healthy, whereas occupations in dusty atmospheres carry a mortality that increases with increase of dust (Fig. 31). In wool-spinning, work like carding, which produces much dust, carries a mortality 48 per cent higher than that in spinning itself; cotton-spinning carries a mortality rate higher by one-sixth over wool-spinning. Some mineral dusts are particularly dangerous. Sand-blasters have a mortality rate three times as high as the normal rate for men, and anthracite miners have a mortality 25 per cent higher than other miners. Occupations involving high temperature carry their own risks: tuberculosis and cancer are between two and two and a half times more deadly to glass-blowers than to the general population. In coalminers the mortality rate varies with the depth of the pits in which they work; bronchitis and pneumonia have a rate 45 per cent higher for workers in deep pits over miners in shallow pits. The mortality rate for accidents varies immensely with different occupations. Against a rate of 100 for all males, it is 37 for cotton weavers, but 295 for builders, and 198-354 for different branches of coal-mining. Among unskilled workers respiratory diseases, including lung tuberculosis, exact a heavy toll.

It is difficult to assess the mass of non-fatal morbidity arising directly from occupations that these mortality statistics imply. It is not merely a problem

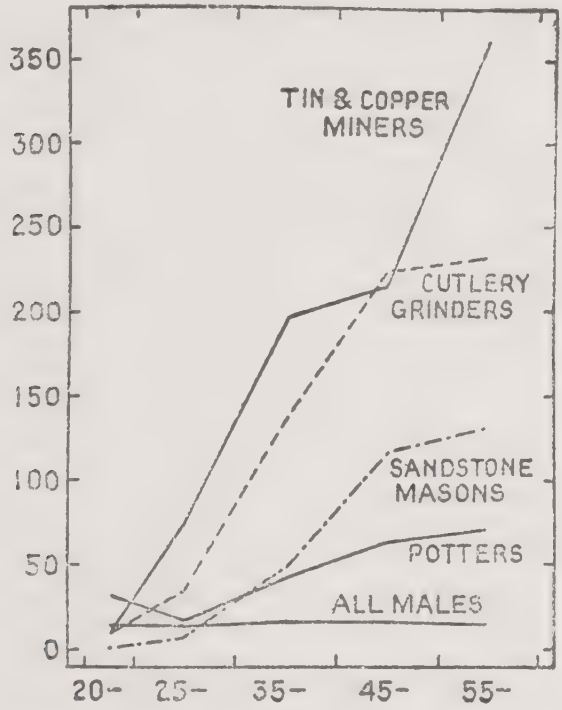


FIGURE 31. OCCUPATIONAL MORTALITY

Mortality from respiratory tuberculosis and allied lung conditions ('chronic interstitial pneumonia') in men in some industries, 1921-3.

Note the even trend of incidence throughout life for men as a whole and the continuously increasing incidence in men at certain occupations.

of the loss of life and all it involves; preceding the gaunt shadow of death there is the grim procession of ill-health, sometimes sharp and stabbing, more frequently insidious and disruptive. Occupational

mortality is indissolubly linked up not only with the actual process of the work, but also with the conditions under which the work is done, the hours of employment, the health of the worker, his home environment, and the incentive to work. Factory Acts have done much to minimize isolated dangers, but have not produced any radical solution.

6. Gross poverty

In tropical countries poverty hangs like a pall shutting out the sun. An equable climate and a fertile soil harnessed to a primitive economic organization operate more favourably for lowly organized life than for man, whose struggle for survival is fierce and raw. Malnutrition is the rule, hunger not uncommon, and famine is always a threatening shadow. The vicious circle of poverty is terribly effective. The low standard of living means endless morbidity, and morbidity in turn means diminished effectiveness in creating better conditions. Man inhabits but does not master the tropical zones of the earth : the mosquito, the louse, the flea, and the rat, among others, hold a stake. Human life flickers rather than leaps like a mountain flame.

Some sixteen hundred million people inhabit these zones, and the extent of morbidity and mortality can be assessed only approximately. It is appalling even in such relatively highly organized countries as British India. The total mortality is over twice that for England and Wales (in 1937, 22.4 per 1,000 against 9.3),

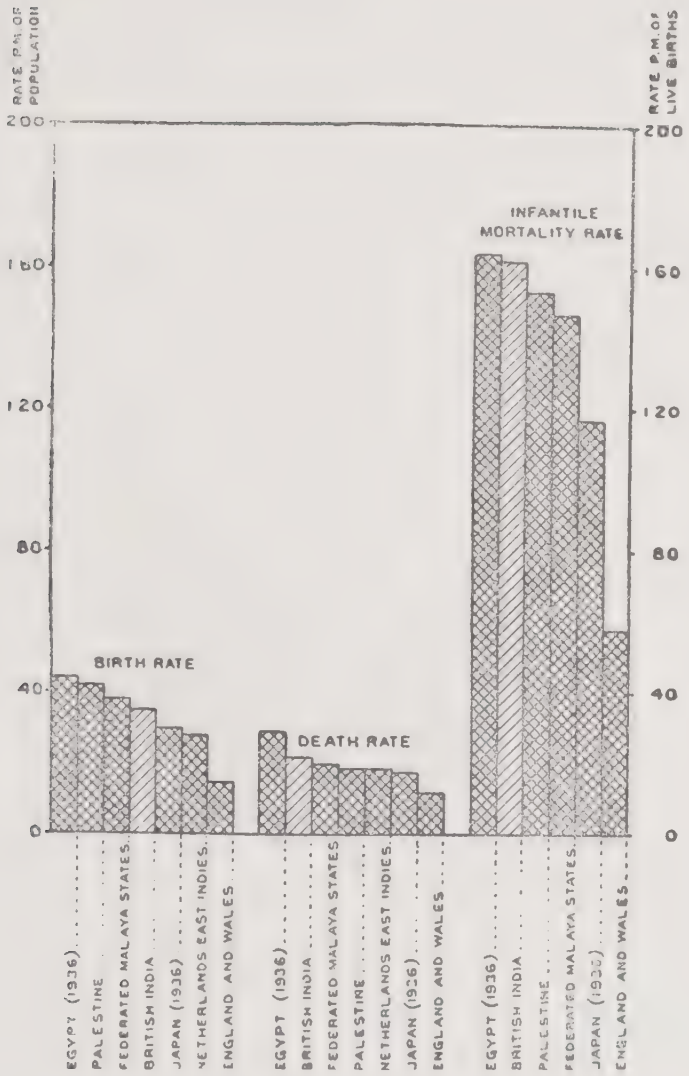


FIGURE 32. A COMPARISON OF BIRTH, DEATH, AND INFANTILE MORTALITY RATES OF INDIA WITH OTHER COUNTRIES IN 1937

infantile mortality is nearly three times as high (161.7 per 1,000 births against 58), and maternal mortality is exceptionally heavy (Fig. 32). About 60 per cent of all deaths are attributed to 'fever', malaria

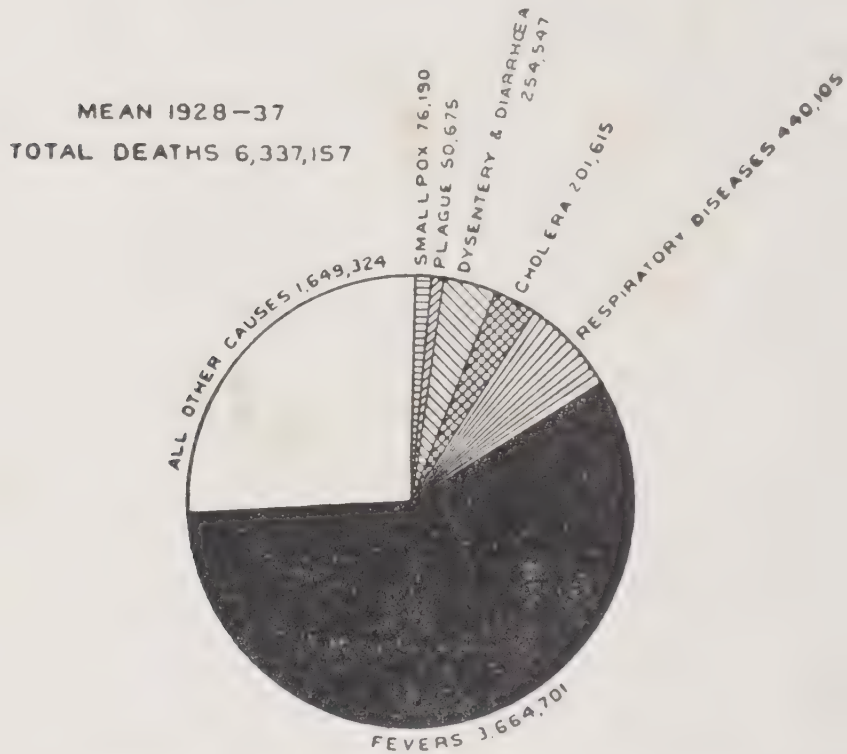


FIGURE 33. FACTORS IN INDIAN MORTALITY

British India—comparative diagram of deaths by causes. There is a heavy incidence of death from 'fevers', mostly preventable.

probably being the largest single factor (Fig. 33). Cholera, smallpox, plague, and dysentery—all conditions that reflect primitive sanitation—exacted a toll of nearly half a million lives in 1937, a fairly typical

year. It is estimated that though ten million Indians are treated for malaria, at least ten times that number are affected; a conservative estimate gives the number of cases of leprosy at one million. The country is infested with deadly affections, the control of which presents no difficulty to medicine—but a high standard of living and vast sanitary schemes are essential. The mortality and morbidity in tropical countries is not 'racial' but environmental; wherever planned reforms are carried through improvement follows.

The social character of much mortality and morbidity among subject races is illustrated by evidence from the U.S.A. and its possessions. In Ohio the mortality rate per 1,000 for the native white male population in 1930 was 10.4 and 20.2 for negro males (the corresponding female rates were 8.5 and 18.3); in the Philippines there was a marked difference in the white and native rates: in Manila in 1919-20 the rates for Americans and Filipinos were 11.8 and 27.4 respectively; in Hawaii, where the Japanese have a social status similar to that of the white population, the rates were 13.9 and 12.4 for these two sections against 39.5 for the indigenous poor population.

In any cosmic book-keeping of life and health poverty is a ruinous luxury.

7. War

If poverty gnaws at life, the elemental fury of war devours it. Medicine must salvage what it can from

the hot furnaces of battle; it must build dykes of sanitation to hold back the pestilence inevitable when massed life is reduced to decay; it must watch the waning vitality of non-combatants. In contrast to the Boer war, there were in the 1914-18 war fewer deaths from typhoid fever than from wounds, and this is reckoned as a triumph of modern medicine. It is also reckoned as a triumph of medicine that the dead from wounds amounted only to millions as against the tens of millions from epidemics—including influenza and famine. By these standards the second world war was a still greater medical triumph—starvation diets, experiments on human beings, gas chambers, and atomic bombs notwithstanding. Mars can afford small change to Minerva.

8. The health of nations

Three-quarters of a century ago one of the architects of English sanitation clearly formulated the conditions necessary before medicine could build national health: 'The public health of a country means the health of its masses, and the masses will scarcely be healthy, unless, to their very base, they be at least moderately prosperous' (Sir John Simon in his Sixth Report to the Privy Council, 1864).

To-day the necessary condition is fundamentally the same, but the problem of its realization infinitely more complex. Victorian England was the scene of unparalleled industrial development, a rising standard of living and an increasing population. To-day

a shrinking population holds out the prospect of fewer effective workers; mass unemployment appears to be a permanent cyclical feature in our industrial system, bringing with it the new phenomenon of depressed areas when migration as an outlet has come to an end. Industrial development no longer pursues an even upward trend, but shows violent fluctuation, with downward tendencies, sometimes controlled, more frequently uncontrolled. The standard of living is no longer rising and there is no faith in the continuous and automatic improvement of things, even if there are periods of advance. The social legislation and the full employment that the aftermath of war has brought are, judging by experience over the last two generations, merely local and temporary. Alternating booms and slumps are not the conditions conducive to public health based on prosperity. Poverty—which is still the lot of all but a tiny fraction of mankind as a whole—has become but one aspect of an acute and widespread social disorder.

The Hippocratic Oath defines nobly the obligations that the physician has to his patient—but these obligations are purely individual and are too narrow for medicine today. Social obligations have emerged, for in the seas of social pestilence there are no Isles of the Blest, only Lotus lands.

CHAPTER X

On the Horizon of Time

1. Emergence of preventive medicine

The dankness of the cemetery hovers around modern medicine. Medicine still looks mainly to healing rather than to the avoidance of disease: this is a negative view of life dictated by the graveyard. Of a positive science of medicine, of the activities by which man consciously and exultingly shapes himself to a dream fashioned in his mind and felt in his heart, there is as yet but the merest glimpse, sensed rather than seen through a too solid darkness.

That darkness is slowly becoming less impenetrable. The triumphs of medicine in understanding and overcoming some of the more crude imbalances that produce disease have made possible not only the saving of much life, but the recovery of normal function as opposed to mere survival. Much of the medicine and still more of the surgery of previous generations was confronted with 'neglected conditions', i.e. conditions which had progressed relentlessly, partly because of personal neglect and a defective medical organization, but mainly because medicine could do little to stem

the ravages of progressive disorders. In this respect modern medicine differs markedly from the practice of even two generations ago.

The halt, the deformed, the deaf, and the blind are the grim procession straggling along the stage of history to testify to the cost at which medicine had succeeded, here and there, in saving life. They are still with us to-day, but their testimony is no longer quite the mass horror it was in days gone by. A healthier race has been built, so that not only the grave, but the lazaretto and the almshouse do not loom so large.

Much the greatest achievement of medicine, so far, is its understanding of the nature of infectious disease. Man has now in his hands the power to overcome the harmful relationship microbial life can establish with him. Sanitation, including such special measures as draining malarial swamps; personal hygiene in its broadest sense; satisfactory nutrition; active and passive immunization—all these are factors that militate against the development of infection. When infection has occurred isolation on clearly established principles, and chemotherapy—the most recent and most significant of all measures—are now available. Gaps still exist; much still remains to be done for a number of specific infections (such as tuberculosis), but infectious disease is no longer an uncontrolled and uncontrollable terror. The microbe is fighting a losing battle.

Yet microbial disease is still widely rampant. Social

inertia is largely responsible for this. This inertia is sometimes administrative, as the mortality from diphtheria shows. Where diphtheria immunization has been carried out on an extensive scale the disease has almost disappeared or lost its deadly character.

Generally more intricate reasons than an administrative failure are the cause of the persistence of infectious disease. Low standards of living still exact a toll through tuberculosis and other respiratory affections, many of the deaths due to 'fever' in the tropics are largely avoidable, as the means of eradicating malaria and many other tropical diseases are known.

2. Cancer and vascular degenerations as outstanding issues

If the eradication of infectious disease may now be considered a realizable aim, this cannot be said of the two major killing affections : cancer and vascular degeneration. Cancer is still largely beyond control except in its early stages, and its importance is measured by the fact that it accounts for one-seventh of all deaths. There is no evidence that the disease is increasing in frequency, but it is assuming a more menacing social character by the fact that it falls heaviest on the age groups of forty-five to sixty-five years (Fig. 34)—a population that has now a more significant position in society owing to the decline in the number of children and the increased expectation

of life for the young adult. In these age-groups it is responsible for one out of four and a half deaths.

Vascular degeneration includes a series of different entities: the failing heart of old age, the rheumatic heart with its onset in childhood, and hardening of

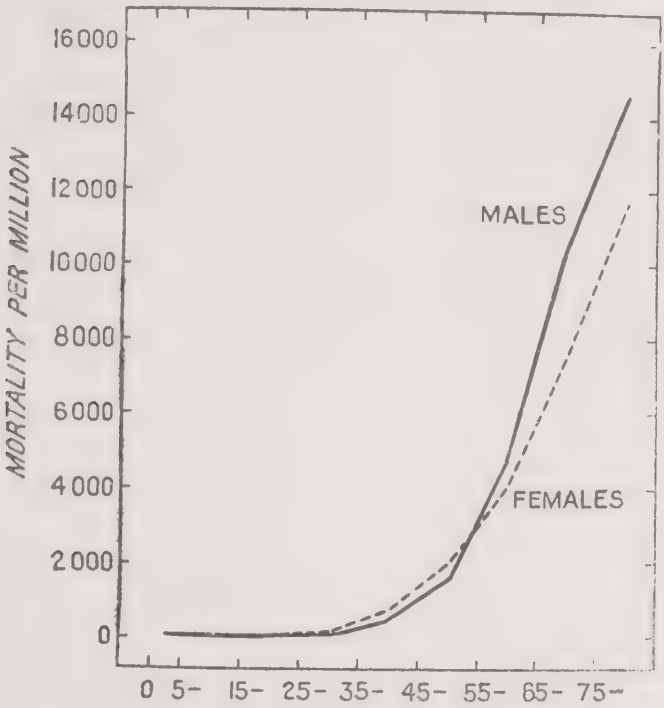


FIGURE 34. CANCER MORTALITY

Mortality rate from cancer in relation to age, 1935.

the arteries (arteriosclerosis), of which coronary thrombosis (narrowing of the arteries supplying the heart muscle) is an important example (Fig. 35). The incidence of coronary thrombosis appears to have increased considerably during recent years, and though the possibility of more accurate diagnosis has

to be considered, the stress of modern life cannot be ignored as a fertile cause of this affection. In the U.S.A., where it is common, arteriosclerosis is regarded as the price of high-pressure life.

Cancer is always a personal tragedy, but vascular degeneration is often a social menace. When hardening develops in the arteries of the brain there is not only physical but also mental impairment. That impairment may take the extreme form of insanity, but more frequently it cripples rather than destroys mental activities. To a mild degree this happens to everyone, as hardening of the arteries is a normal process of ageing. The rigid outlook of the middle-aged reflects the rigidity of their cerebral vessels, and in a society in which there are fewer young people to elbow out ossifying men who lead by virtue of their age, the danger of social life becoming an unadventurous existence is real.

Medicine, as yet, has no clear answers to the problems of cancer and vascular degeneration. With the all but complete solution of the problem of infection, which in previous generations dominated medical thought, cancer and vascular degeneration have become the outstanding problems of contemporary medicine. They are the two narrow passes in which middle-age is often slaughtered—passes which medicine has to widen into highways leading to the reposeful and satisfying plains of normal old age.

3. The social pre-requisites for healthy development

A normal old age can derive only from a normal life, and the possibility of a normal life depends on the elimination of all those factors that are discordant

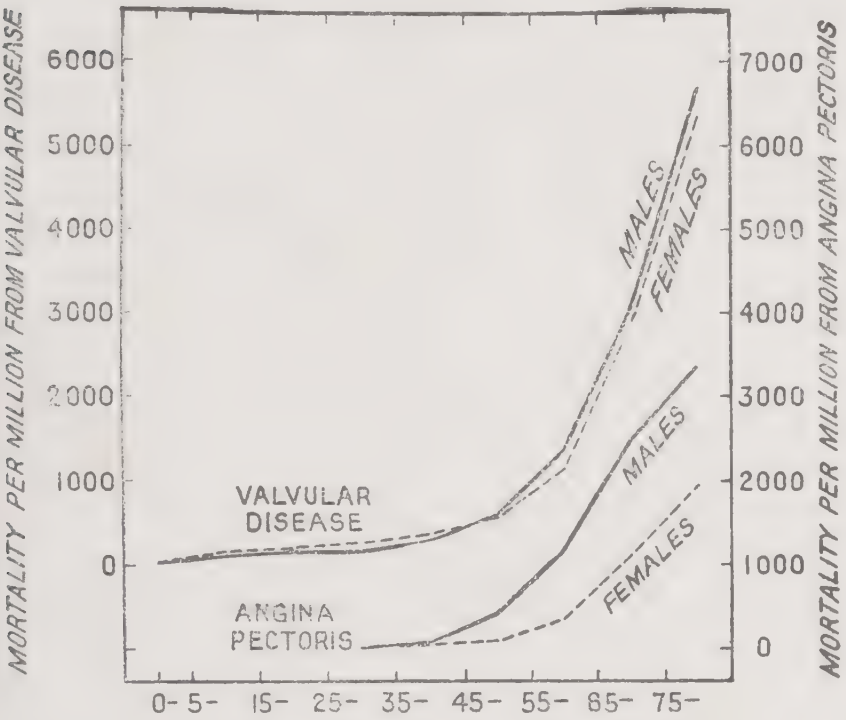


FIGURE 35. MORTALITY FROM VASCULAR DISEASE

Mortality rate from heart disease in relation to age. 1935.

to normal development. The creation of such conditions cannot be achieved by medicine or by any other single human agency. It is a task calling for extensive and co-ordinated effort.

Human pathology is indissolubly linked up with social pathology. In a society in which there is war

and its consequences the conditions do not exist for active life mellowing into old age. In cities built haphazardly, the mansion and the slum are corollaries. Where the horror of street upon street of back-to-back hovels is tolerated there is unlikely to be any appreciation of the need for parks and open fields. As long as the individual worker is the most cheaply replaced component of industrial stock, his welfare is not likely to be the first consideration in production: factories will continue to be built and mines sunk to satisfy other reasons than the dictates of life and health. The production of goods and food geared to any other motive than their consumption by the producers must lead to the insanity of food being burnt or stored, and manufacture restricted or diverted for war at a time when there is widespread malnutrition and want with all their consequences on health. Morbidity and mortality directly arising from poverty and social mismanagement in a society that has technologically solved the needs of production, present to medicine not a problem but an outrage. Medicine is not a veterinary science concerned with maimed, ill-treated, and badly cared for human herds.

4. The control of genetic disease

In hereditary disease medicine can as yet act only as an inefficient scavenger. The recognition of dominant inheritance in a relatively small group of severe defects and disorders still beyond treatment suggests

the eradication of such disturbances by controlled reproduction. Sterilization—statutory or voluntary—of individuals exhibiting disabling dominant affections is the most radical of a variety of possible measures, which include abstention from marriage, contraception, and legalized abortion. Since recessive disease is more common than dominant affections, such measures have a strictly limited application unless genetic diagnosis develops methods of disclosing adverse recessive characters in apparently normal individuals. At the present only the birth of one or more children with a recessive disease is the means of establishing recessive disease-bearing factors in both the parents. With the widespread distribution of such factors in the general population little can be expected in the control of recessive disease by methods which are efficient in dominant hereditary affections. Moreover, in some apparently recessive conditions (such as mental deficiency) it is not always possible to exclude environmental factors. The limits of genetic control of recessive disease are seen from the estimate that it would take some seven hundred years to reduce the incidence of recessive mental defect from its present ratio of 3 per 1,000 to 1 per 1,000. Eugenics as usually expounded has little relevance to the immature science of human genetics; it is not the progeny of genetics, but a dysgenic foundling left at its doorsteps.

Genetic measures calculated to improve racial vitality by selective marriage are little more than

an unintelligent aping of natural selection. On the avoidance of dysgenic marriages involving the danger of the perpetuation of physical defects there is a tangible basis for action. This is not so for marriages calculated to perpetuate some supposed mental or physical advantage. Such proposals are based on the assumption, frequently unproven, that given characters are genetic and not environmental: they also overlook the fact that man is a tangle of physical and mental qualities and that consequently the ideal of perfection in man is infinitely more complex than that of perfection in animals reared for a particular quality. Selective marriages reach their logical conclusion in proposals for artificial insemination as the best method of racial perpetuation. That such measures would produce a highly selected race cannot be doubted; what is open to question is that the qualities selected would bear any resemblance to the narrow ideal conceived by the selectors. The irreplaceable raw material of variation in life can hardly be entrusted to contemporary man. It is not in the impatient destruction of such raw material, but in the understanding of its nature, that further progress lies—all the more so since the progress of genetics has rendered meaningless any sharp antithesis between heredity and environment, between nature and nurture.

The gene as the basis of hereditary transmission is no longer regarded as a rigid building-stone, changeless and immutable. The inherent instability of the

gene as shown by mutation; the interaction of genes among themselves, so that the sum total of gene effect rather than the action of a single gene is the ruling condition for the emergence of particular features; and the determining action of environment on the manifestation or non-appearance of gene effect: all these have revealed hereditary transmission as a plastic force. The gene is not a baked brick, but building clay of varying plasticity.

Human genetics has so far been concerned mainly with the elucidation of single gene effects that are apparent under a wide range of environmental conditions, and such studies constitute the classical examples of hereditary disease. Yet modern genetics illustrates forcibly that the classical conception of hereditary disease concerns only a limited group of conditions in which the hereditary features are of considerable (but not absolute) rigidity. In a comprehensive view less rigid hereditary features that are more easily modifiable are just as significant.

In animal genetics the significance of environment as an interacting force with the gene is clearly established. Some chickens have white shanks and others yellow shanks; chickens having either feature can be bred true to form, so that the difference is genetic and not environmental. Yet if chickens that genetically are of the yellow-shank variety are fed not on green food, but on white corn, their shanks are white. The gene effect is suppressed by easily controlled environmental factors; or, to put it differently the

gene effect can become manifest only under environmental conditions that include green food. Similarly there are rabbits that have yellow fat and rabbits with white fat; these too are genetic differences, but rabbits that genetically are of the yellow-fat variety will deposit white fat if their food lacks greenstuffs. Tadpoles are genetically destined to become frogs, but if tadpoles are kept in water and on a diet in both of which there is no trace of iodine they never fulfil their genetic destiny; their thyroid mechanism, which determines the change from tadpole into frog, cannot function in the absence of the environmental factor represented by iodine. Similarly a local race of the American newt, found in the neighbourhood of Mexico City, never grows up. It breeds from generation to generation in the aquatic form, but will become a terrestial newt if fed on thyroid gland (Fig. 36). Here a genetically determined capacity can be released by an environmental factor represented by the secretion of the thyroid gland (thyroxine). A further example is the variety of domestic fowl known as the Frizzle, a bird practically devoid of feathers throughout the first year of life, and so delicate that it is difficult to rear. The pure Frizzle will become more hardy and develop a complete plumage within three weeks if it is reared in a woollen jacket and kept in a warm room.

The evidence of experimental embryology on the modifiability of hereditary tendencies by extraneous factors is further proof of the lack of rigidity of

hereditary material. In human pathology a similar effect is illustrated by the greater frequency of mongolism and congenital abnormalities as a whole in the children of ageing mothers: some change in intra-

FIGURE 36. AXOLOTLS

A has not been treated.

B has received thyroid extract. Note the disappearance of the gills and of the fins from the tail.

The axolotl is normally a water animal—a sort of frog remaining in the tadpole stage. If fed on thyroid gland it develops air-breathing organs and becomes a land animal.

uterine environment is here the determining factor. The control of Niemann-Pick disease by a fat-limited diet and of diabetes by insulin illustrates the suppression of genetic manifestations by environmental influences after birth.

The sum total of gene effect in modifying the

simple action of a single gene is strikingly shown by an observation on fishes. Different varieties of the Mexican kill-fish possess large black pigment cells, small black pigment cells, or no pigment cells at all. These are genetic differences, and crosses between the two genetically distinct varieties with black pigment cells produce offspring distinguished not only by pigment but also by the presence of tumours.

Genetics has thus travelled far from the acceptance of hereditary characteristics as immutable entities. It has opened up prospects of modifying human heredity by suitable environmental action on genes. Hereditary disease, which even now is influenced by treatment in a limited group of affections, may well prove to be within human control. And more, it may prove to have indicated the way by which man, gaining knowledge of his building clay, will learn the secret of the evolution of a race of gods.

5. The chemistry of health

Chemicals are likely to be the hammers and engravers of man's plastic building material. As yet more is known of the action of hormones on the development of the body and of the interaction between various ductless glands than of the conditions necessary for the development of the hormones themselves. That iodine is essential for the production of thyroid secretion is established, and there is much work in progress on the role of vitamins in stimulating hormone production. Beyond the vista of correcting hormone

imbalances which produce a whole host of major and minor disturbances, lies the alluring prospect of controlling gland action to the extent of inducing new physical and mental qualities in the adult and still more in the embryo. The new-born child is already largely a finished product, having been influenced for nine months by the environmental factors of his mother's personality. As opposed to the mere avoidance of cretinism in the newborn by supplying the mother with sufficient iodine, and the prevention of congenital syphilis by treating an infected mother during pregnancy, medicine may be able to build the embryo's personality as desired by controlling its maternal environment and its own endocrine system. The method of tissue culture which has developed to the stage where whole organs, including the pregnant womb, can be kept alive outside the body, opens this vast prospect, as it will become possible to study the effect of medication on evolving life. The largely uncontrolled maternal environment which the womb gives to the embryo may be replaced by a scientifically determined environment. A man-made environment for the growing child can boast of great achievements in reducing infantile mortality and morbidity; what a man-made environment for the more malleable growing embryo may achieve is one of the tantalizing riddles of the future. And beyond this lies the prospect of rearing the fertilized human ovum outside the womb (ectogenesis)—a prospect with incalculable effects on the child-bearing half of the human race.

Drug addiction may become a normal feature of life, except that it will not be addiction or drugging in the present-day sense. The linked effects of stimulation and depression that both alcohol and cocaine possess may be dissociated so that only stimulation, mental and physical, will be produced. The cup of tea or coffee of to-day, the tonic, and the present tentative production of non-habit forming, stimulant chemicals, may well develop into a gearing mechanism for life's activities. Chemistry may yet serve normal man as well as it is serving him to-day by chemotherapeutics in infection. It will undoubtedly modify diet, but it is unlikely to evolve 'tabloid' food, for man will not readily abandon the primitive delight of eating.

6. Beyond tissue culture

The culture of whole organs represents a synthesis of anatomy, physiology, cellular integration, and biological time. A living organ, may now be studied under conditions that can be varied at will by the experimentalist, and the conditions under which life activities can be modified are now open to direct observation for prolonged periods. By modifying the fluid in which the organ is placed, it is possible to observe directly what previously could only be inferred. The normal life of an organ can be studied in respect to conditions that accelerate it or slow it down, and the process of healing is now subject to direct experimental observation. It may prove that

optimum conditions for the healing of a diseased organ can be obtained more easily when the organ is removed from the sum of influences within the body, and Alexis Carrel has visualized the time when a thyroid extirpated in the course of an operation, or a kidney removed for tuberculosis, or an amputated leg, would be restored to normality and replanted in the body: isolated diseased organs, rather than patients, would be treated in the hospitals of the future. When the body as a whole dies, a mass of living tissue will be still available for study and use. Skin grafting as practised to-day for the loss of tissue, and corneal grafting for the restoration of sight, may prove the beginning of a new surgery concerned with the replacement of worn-out parts; the logical development would be the stringing together of a synthetic man of finer parts and fewer patches.

7. Life and death

Whether life slowly ebbs by an inherent rhythm to a ripple that ends by breaking on the shores of oblivion and decay, or whether it is disrupted insidiously by a thousand and one marauders that have broken into the citadels of the body, is a fundamental problem to which there is no answer. If death is indeed accidental to the mode of life rather than inherent in life itself, the Psalmist's three-score years and ten must have represented in ancient Judea as wild an aspiration as it is a sad underestimate of the possibilities in the world of to-day. In primitive

society life was not only nasty and brutish, but also short. From inscriptions on Roman tombstones it is estimated that the mean length of life in antiquity was somewhere between twenty and thirty years (as it is in India to-day). For the city of Breslau in 1687-91 it was computed as 33.5 years. In Sweden it was 34.5 for 1755-76, rising to 41.5 for 1816-40, and since then steadily to 62.3 for 1925-30. In other highly organized countries the trend has been the same. Expectation of life in England rose by over twenty years between 1854 and 1935-7 (from 39.9 to 60.17 for males, and from 41.85 to 64.35 for females); for the white population of the U.S.A. it rose by about ten years between 1901 and 1929-31.

This increase in expectation of life at birth reflects chiefly the great reduction in infantile mortality, for the lengthening of life at higher ages has not been marked. In the U.S.A. in the thirty years between 1901 and 1929-31 the increased expectation of life of people aged forty years was only 0.74 years. In England it was rather more—about four years in the past sixty years for people aged forty-five (the male rate in 1871-80 was 22.07 and 25.53 in 1935-7, the corresponding female rates being 24.06 and 28.59). The absence of any marked increase in expectation of life at higher ages may be due to the fact that the decline in infantile mortality has increased the proportion of people who die prematurely not in infancy but later on in life; a more important factor is the failure to influence to any marked extent the incidence of cancer and

vascular degeneration, the two major killing diseases in middle-age. It has been computed that the expectation of life at birth would have been 7.2 years more in 1930 in the U.S.A. if there had been no deaths from cardiovascular-renal diseases. Geriatrics, the study of the diseases of old age, as opposed to paedriatics, the study of children's diseases, is overdue for a place amongst the specialities of medicine. Much more has to be learnt of the normal processes of ageing before 'rejuvenation' becomes a practical procedure; it is unlikely to be just a question of grafting some gland tissue.

Lengthening of life is thus as yet largely a matter of eliminating the avoidable causes of death. Much may be expected from the ultimate conquest of cancer, the diminution of deaths from infectious diseases (including tuberculosis and syphilis) and from the reduction of deaths due to industrial diseases and accidents, and a variety of other causes that take a heavy toll of the middle-aged and the ageing. The most significant advances must, however, come from the conscious building of a stable society with raised standards of living and from medical activities culminating in the eradication of cancer and cardiovascular degeneration.

With the abolition of preventable causes of death, the normal span of human life would probably be nearer a century than the proverbial three-score years and ten. As knowledge accumulates on the cycles and rhythm of life, the biological problem of causation of

death—as distinct from the pathological factors leading to death—emerges as a crucial issue. Death is not universal. The germ plasm itself is inherently immortal; and the millennia that some trees have lived, as also the fact that death as an inescapable biological destiny hardly exists in protozoa and some insects, raise the question of the mechanics of death in man. There is a variable rate of ageing in different tissues: the most highly developed tissues in man—the brain and sense organs—show fewer senescent changes than the phylogenetically more ancient systems of the body, such as the skeleton and the cardiovascular system. The rhythm of life appears to be the determining factor in ageing. Thus both in plants and animals experimental evidence shows that if growth is controlled life can be extended (Plate I, Fig. B). Monocarpic plants (plants that die after bearing one crop of seeds) kept under conditions that prevent flowering can be made to continue in their vegetative form, i.e. their life span is extended indefinitely and the ageing effect of flower and seed production prevented. The normal span of life of the white rat is 600 days. If young rats are fed on a diet adequate for maintenance but insufficient to permit growth, a life of 1,000 days may be reached. Retardation of growth is, however, only one of the possible methods of lengthening the span of life. Other nutritional experiments indicate the significance of various food factors in curtailing or extending life, but they do not dispose of the possibility that such experimental conditions merely

bring out that the usual mode of life is inimical to the attainment of the full span of life. The same objection hardly applies to the experiments in slowing up growth; and the fact that in those animals with greatly prolonged life degeneration of the vascular system occurred early in life more frequently than in normal control animals, raises the puzzling issue as to what extent vascular degeneration, which is generally regarded as a normal factor in ageing, is after all a pathological process. To-day less than ever can medicine give a categorical negative to man's nostalgic quest for youth perennial and life eternal.

8. Conscious evolution

Evolving out of formless matter from which the blind forces of mutation and natural selection have fashioned him, man, simian *homo sapiens,* exercising his prerogative of thought, has created human purpose as a new force. He has drawn sharp boundaries for other life than human, and has extended the limits of human life to regions natural selection barred to him. By creating a man-made evironment he is placing his own well-being as the highest good in the scheme of things, scorning to let it be an incidental result in the activities of nature. The slave has been ennobled by the joy of creative effort. No longer a helpless plaything of the gods, he is becoming a legislator of the universe. But this half-ape, half-god is still in the grip of his own defects, and in throwing off the clamps of circumstance he is learning to look

into himself. He that is already moulding the forces that have made him is unlikely to rest content with the faulty product of their haphazard efforts. And it is not the shape and mind of Caliban that looms on the horizon of time.

Glossary

Abiotrophy. A genetically determined decay of fully developed cells or tissues.

Acetone Bodies. Incompletely oxidized products of abnormal fat metabolism.

Alimentary Canal. The tube within which digestion and absorption of the food takes place; it extends from the lips to the anus.

Allergy. An altered reaction of the body, in which the patient reacts in a manner differing from the primary reaction to the subsequent introduction of the same substance into the body.

Amino-acid. An organic acid in which a hydrogen atom has been replaced by NH_2. It is one of the products of the hydrolysis of proteins.

Amniotic Fluid. The fluid contained within the amniotic sac, which is the inner membrane of the sac surrounding the foetus and adherent to the wall of the womb.

Analgesic. A remedy applied for the relief of pain.

Anaphylactic Shock. An increased susceptibility to the

action of a foreign protein, following its previous introduction into the body.

Aneurysm. A localized dilatation of the wall of an artery or vein.

Antibody. A substance produced in the body which exerts a restrictive or neutralizing effect on bacteria or other harmful substances.

Antigen. A substance which after introduction into the body causes the production of antibodies.

Antitoxins. Substances produced in the body which counteract the effect of toxins.

Asepsis. Freedom from disease-producing organisms. Antisepsis, in contradistinction, involves the destruction of organisms already present.

Autonomic Nervous System. A subdivision of the general nervous system, which deals with autonomic bodily activities, e.g. movements of the intestines, circulation, etc. It consists of two parts—the sympathetic and parasympathetic—the actions of which are largely antagonistic, e.g. the former if stimulated increases the rate of the heart, the latter reduces it.

Bacillus (plural, bacilli). A type of micro-organism, characterized by its rod shape.

Bactericidal. That which proves fatal to bacteria.

Basophile. A cell or other element possessing an affinity for basic or nuclear stains.

Carrier. (1) A person who is apparently healthy and

who harbours organisms capable of producing disease in others. (2) An apparently healthy person who carries a recessive genetic character.

Cell. A granular mass of protoplasm containing a nucleus. It is the living basis of all plant and animal organization.

Cerebro-spinal Fluid. The fluid surrounding the brain and the spinal cord.

Chromosome. A body visible in a nucleus during cell division. It carries the genes. Chromosomes generally go in pairs.

Coccus (*plural,* cocci). A type of micro-organism, of spheroidal form.

Cold-blooded. Varying in temperature with that of the surroundings.

Colon. The large bowel or large intestine.

Cornea. The transparent membrane forming the front portion of the outer coat of the eyeball.

Cortex. The outer layers of certain organs, as distinguished from the core (medulla).

Cortin. A substance extracted from the cortex of the suprarenal gland.

Culture. (1) The growth of organisms on artificial media, e.g. agar jelly, potato. (2) The growth of cells, tissues and organs in nutrient media.

Decompression. Removal of pressure. Often applied to an operation on the skull to relieve the increase

of pressure on the brain, due to a space-occupying mass, e.g. brain tumour.

Diencephalon. A portion of the brain uniting the mid-brain with the fore-brain.

Dominant. An hereditary feature that is expressed even if only one of the two genes carries the factor for determining that feature.

Duodenum. A horse-shoe shaped portion of the alimentary canal, connecting the stomach with the small intestines.

Dwarfism. A state in which the subject is markedly undersized. Sexual development proceeds normally.

Ecology. The study of the relationships of living organisms with their environment.

Empiricism. Practice founded on experience.

Endemic. The constant prevalence of an infectious disease in a community.

Endocrinology. The study of the endocrine glands, i.e. those glands which produce an internal secretion that is absorbed directly into the blood.

Enzyme. A chemical ferment, secreted by the body cells, which induces chemical changes in other substances by catalysis, itself remaining unchanged during the process.

Eosinophile. A cell or other element which stains readily with eosin, a coal-tar product employed as a dye.

Excretion—see Secretion.

Fistula. An abnormal channel, one end of which communicates with the exterior, the other with the cavity of a hollow organ.

Foreign Body. A term used to describe an extraneous substance in a wound, organ, or cavity.

Gene. The unit of heredity carried by the chromosomes.

Genetics, The study of heredity.

Germ Plasm. The part of a germ cell containing the hereditary matter (chromosomes).

Gigantism. Tendency towards the build of a giant.

Gland. An organ that produces a secretion.

Glycolysis. The process by which sugar is chemically broken down in the body in readiness for absorption.

Goitre. An enlargement of the thyroid gland, due to other causes than infection or new growth.

Gonococcus. The specific organism that causes gonorrhoea.

Habitat. The place where a species of animal or plant is found in nature.

Histology. The study of the cell structure of tissues.

Homeopathy. A system of medical treatment by small doses of drugs which in larger doses would produce symptoms similar to those of the disease being treated.

Hormone. A chemical substance formed in one organ

and carried by the blood to stimulate various activities elsewhere in the body.

Host. The organism upon which a parasite lives.

Hypothalamus. An area of the brain lying below the thalamus.

Immunity. A state, natural or acquired, in which the body is resistant to disease.

Infantilism. A cessation of the physical development at an early stage, including arrest of sexual growth.

Insemination. The deposition of semen in the vagina.

Intestine. The digestive tube extending from the stomach to the anus.

Lipoid. A type of fat.

Medulla. The central portion of certain organs, as distinguished from the external part or cortex.

Metabolism. The complex chemical changes whereby foodstuffs are transformed into living matter (anabolism) and whereby protoplasm in converted into simpler substances to perform special functions (katabolism).

Miasma. Noxious effluvia or emanations.

Morbid. Relating to disease.

Mucous Membrane. A membrane that secretes mucus (a clear, viscid fluid) lining cavities and canals that communicate with the exterior.

Mutation. A change in a unit of heredity. May be accompanied by visible changes in a chromosome.

Nucleus. That particular portion of the cell that is the executive centre for the activity of the cell. It differs in structure from the rest of the cell.

Nutrient medium. The substance on which living tissue such as microbes or organs are developed.

Oestrin. The internal secretion of the ovary.

Optimum. The most favourable conditions possible.

Organ. Any part of the body exercising a specific function, as of digestion, etc.

Ovum. The female sexual cell or egg.

Pandemic. Epidemic of world-wide dimension.

Pathogenic. Disease-producing.

Phylogeny. Evolutionary history of a plant or animal species.

Pituitary Gland. A small endocrine gland situated in the hollow of a bone in the base of the skull and connected to the brain.

Placenta. The structure connecting the embyro with the mother. One side is attached to the wall of the uterus and the other to the child by means of the umbilical cord.

Proteins. A group of chemical substances containing carbon, hydrogen, nitrogen, and oxygen, among others. They constitute the chemical basis of living tissue.

Puerperium. The period immediately succeeding childbirth.

Quarantine. The detention of ships and their passen-

gers, or humans and animals, during the incubation period of an infectious disease to which they may have been exposed; the segregation of the subject of an infectious disease during the period of infectivity.

Recessive. A hereditary feature that is expressed only when both of the two genes that determine a character carry it. Opposite of dominant.

Schick Test. A skin test to determine susceptibility to diphtheria.

Secretion. The product of cellular or glandular activity. It is stored up or utilized in the body, thereby differing from an excretion intended to be expelled from the body.

Sensitization. Rendering cells or tissues more sensitive to the action of an agent.

Serum. The clear, yellow fluid obtained after clotting of the blood. It is also applied to serum containing antibodies for therapeutic use.

Sphincters. Circular muscles that guard the orifices of the body, opening or closing with varying requirements.

Spirochaete. Organisms of a slender, wavy form, capable of movement. *Spirochaete pallida* is the organism of syphilis.

Staphylococcus. A variety of the coccal type of microbe occurring singly, or in masses which resemble a bunch of grapes.

Streptococcus. A variety of the coccal type of microbe

consisting of spherical organisms arranged in chains.

Streptococcus haemolyticus. Streptococci that have the capacity to break up red blood corpuscles. They are the causal organisms of affections like erysipelas, scarlet fever and puerperal sepsis.

Suprarenal Gland. A small, triangular shaped organ situated on the upper pole of each of the kidneys.

Syndrome. A collection of symptoms and signs, not confined to one organ, which together constitute the picture of a disease.

Therapeutics. The art of treatment.

Thyroid Gland. An endocrine organ situated at the base of the front of the neck.

Tissue. A collection of cells or their products which form a definite structure.

Toxins. The poisonous substances produced by microbes whereby they exert their deleterious action on the body.

Toxoid. A modifed form of toxin, used for the production of specific defensive substances in the body.

Trachoma. A widely prevalent infectious eye disease causing much blindness throughout the world.

Trypanosomiasis. Infection by trypanosomes, rather large protozoan parasites, responsible for many tropical diseases of which tropical sleeping sickness is an example.

Tuberculin Test. A specific test for which the products are derived from the bacillus of tuberculosis, a positive reaction indicating past infection.

Vaccination. (1) The injection of the virus of cow-pox as a protection against smallpox. (2) The injection of modified forms of organisms for the purpose of stimulating the production of antibodies.

Vaccine. Modified and weakened pathogenic organisms which, when introduced into the body, result in the building up of defence mechanisms.

Venesection. The opening of a vein for the purpose of removal of blood ('blood-letting').

Virilism. The appearance in women of secondary sexual features of masculine nature.

Virus. Ultramicroscopic organisms responsible for some diseases, e.g. influenza and poliomyelitis.

Warm-blooded. Containing a mechanism that keeps animals at an even temperature.

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